Determination of Photolytic Degradation of Anzet (Flupentixol-Melitracen)

Chowdhury Shafayat Ibne Kamal

ID: 2008-3-70-066

Department Of Pharmacy

East West University

Research Invigilator: Mr. Anisur Rahman, Lecturer.

A thesis report, submitted to the Department of Pharmacy, East West University, in partial fulfillment of the requirements for the degree of Bachelor of Pharmacy

DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation, entitled "Determination of Photolytic Degradation of Anzet (Flupentixol-Melitracen)" is an authentic and genuine research work carried out by me under the guidance of Mr. Anisur Rahman,Lecturer, Department of Pharmacy, East West University, Dhaka.

_____

Chowdhury Shafayat Ibne Kamal

ID: 2008-3-70-066

Department of Pharmacy

East West University, Dhaka.

CERTIFICATE BY THE INVIGILATOR

This is to certify that the dissertation, entitled

"Determination of Photolytic Degradation of Anzet (Flupentixol-Melitracen)" is a bonafide research work done by Chowdhury Shafayat Ibne Kamal, in partial fulfillment of the requirement for the Degree of Bachelor of Pharmacy.

_____

Mr. Anisur Rahman

Lecturer

Department of Pharmacy

East West University, Dhaka.

ENDORSEMENT BY THE CHAIRPERSON

This is to certify that the dissertation, entitled

"Determination of Photolytic Degradation of Anzet (Flupentixol-Melitracen)" is a bonafide research work done by Chowdhury Sahafayt Ibne Kamal, under the guidance of Mr. Anisur Rahman, Lecturer, Department of Pharmacy, East West University, Dhaka.

_____

Dr. Sufia Islam

Chairperson and Associate Professor

Department of Pharmacy

East West University, Dhaka.

ACKNOWLEDGEMENT

I express my profound gratitude and deep respect to Mr. Anisur Rahman, Lecturer, Department of Pharmacy, East West University, for his expert and careful guidance, sincere help, constructive criticism, valuable time and honored suggestion without which I would not have been able to complete this work. He had been very enthusiastic and supportive in my research.

It is my great pleasure and privilege to acknowledge my deepest regards and gratitude to Dr. Sufia Islam, Chairperson and Associate Professor of the Department of Pharmacy, East West University, for her kind words during my troubling moments, and of course for her approval of the topic, constant inspiration and whole hearted cooperation.

I am also grateful to Dr. Repon Kumar Saha, Assistant Professor, Department of Pharmacy, East West University, for his sincere helps, valuable time and honored suggestion which actually carved the path of our research.

I am thankful to the laboratory instructors Mr. Sujit Kumar,Mrs. Razia Sultana and Mrs.Tania for their kind support during the laboratory work.

I wish to thank my fellow researchers namely Ikhtiar Ahmed, Nakib Ibne Omar, Nigar Sultana and Sabbir Ahmed for their endless cooperation and inspiration for preparing this work.

I also like to thank my family members for their support and inspiration to complete this work.

Above all, I express my gratitude to Almighty Allah for giving me the strength, energy and patients to carry out this research work.

TABLE OF CONTENTS

CHAPTER 1: INRODUCTION

Chapter Two: LITERATURE REVIEW

List of Contents **Page No.**

CHAPTER 3: MATERIALS & METHODS

List of Contents **Page No**

CHAPTER 4: RESULTS & DISCUSSION

List of Contents **Page No**

LIST OF TABLES

Table No. and Title **Page No.**

LIST OF FIGURES

No. Name of the Figure Page No.

No. Name of the Figure Page No.

No. **Name of the Figure** **Page No.**

No. Name of the Figure Page No.

Dedicated to my parents and my all teachers

Abstract

This research work was aimed to the determination of photolytic degradation of Flupentixol-Melitracen combination products. The objective experiment is to determine the effect of Flupentixol-Melitracen combination products in various conditions (control, sunlight, normal light, 25watt and 40watt light condition). Physical tests were performed for evaluation of hardness, thickness, weight variation, friability, of the Anzet tablets from same batch. Physical tests were performed according to the specification of USP and BP. But it was observed that the concentration of Flupentixol dihydrochloride and Melitracen hydrochloride was decreased gradually in various light condition like under 25 and 40 watt electrical bulb, sunlight exposure condition. So we can say that the Anzet containing combination of Flupentixol dihydrochloride and Melitracen hydrochloride is light sensitive and the potency is decreased after light exposure

Keywords: Potency, Anzet, Batch, Thickness, Weight variation, Percent friability, USP, BP.

Chapter One

INTRODUCTION

1.1ANTIPSYCHOTIC

1.1.1 Definition

An antipsychotic also known as neuroleptic is a tranquilizing psychiatric medication which is used to treat psychosis, schizophrenia and bipolar disorder. Now it is increasingly being used to treat the non-psychotic disorders. Psychosis disorder included delusions or hallucinations. Delusion is the pathological condition that is the result of an illness or progressing of illness. A first generation of antipsychotics was discovered in the 1950s which is known as typical antipsychotics. Atypical antipsychotics have been developed as a second generation drug recently. Clozapine was the first atypical antipsychotic drug which was developed in 1950s. Clinically it was introduced in the 1970s. Both generations of the drug have the ability to block the dopamine receptor present in the brain.

1.1.2 General Mode of action of antipsychotic Drug

All antipsychotic drugs gives psychotic effect by blocking D2 receptors (Dopamine receptors) that is present in the brain cells. Excess amount of dopamine is released through mesolimbic pathway that has been linked to psychotic experiences. Blocking the dopamine receptor by this pathway is thought to control psychotic experiences. Typical antipsychotics also block the dopamine receptors through several pathways like nigrostriatal pathway, mesocortical pathway, and tuberoinfundibular pathway.

Atypical antipsychotic drugs also block the dopamine receptor (D2 receptors). Some atypical antipsychotic drugs also block the 5HT2A, C and 5HT1A receptors which are known as serotonin receptor. By blocking the serotonin receptor helps to prevent the negative symptoms of schizophrenia.

2. OVERALL OBJECTIVE OF THE RESEARCH

The objective of the research project is to determine the photolytic degradation of Flupentixol-Melitracen combination products. In our research we conducted experiment to

determine photosensityvity of Flupentixol-Melitracen combination products in various lightening conditions (control, sunlight, normal light, 25watt and 40watt light condition).

3. FLUPENTIXOL-MELITRACEN

1.3.1 Flupentixol-Melitracen combination

Flupentixol-Melitracen is a combination preparation of two well known and time tested molecules: Flupentixol and Melitracen. Flupentixol is a neuroleptic with anxiolytic and antidepressant properties when given in small doses and Melitracen is a bipolar thymoleptic with activating properties in low doses. In combination the compound renders a preparation with antidepressant, anxiolytic and activating properties and mutually neutralizes side effects (Popular 2012). In this research project experiment conducted on sample which was manufactured by Popular Pharmaceutical Ltd (Brand Name: ANZET).

Figure 1.1: Picture of Sample-Anzet(Flupentixol-Melitracen)

1.3.2 Flupentixol Hydrochloride

Molecular Formula $C_{23}H_{25}F_3N_2OS$, 2HCl. Flupentixol dihydrochloride is white or almost white powder and chemically it is known as2-[4-[3-[(*EZ*)-2-(trifluoromethyl)-9*H*-thioxanthen-9-ylidene] propyl] piperazin-1-yl] ethanoldihydrochloride. 507.44 is its' molecular weight. It is very soluble in water, soluble in alcohol, practically insoluble in methylene chloride. (British pharmacopoeia 2009)

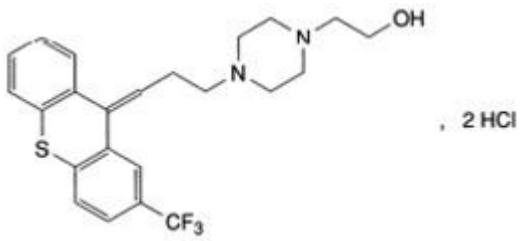

Figure 1.2: Molecular Structure of Flupentixol dihydrochloride

1.3.3 Melitracen hydrochloride

Molecular Formula of Melitracen hydrochloride is $C_{21}H_{25}N.HCl$. Melitracen hydrochloride is a white to off white powder and amorphous in nature and chemically it is 3-[10, 10-Dimethyl-9(10H)-anthrylidene]-N, N-dimethylpropylamine hydrochloride. Its molecular weight is 327.90 (Chemblink 2012).

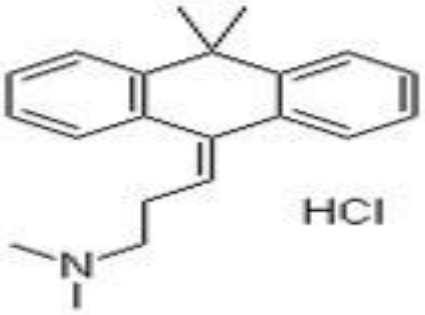

Figure 1.3: Molecular Structure of Melitracen hydrochloride

Melitracen hydrochloride is a tricyclic antidepressant. Thus it works by inhibiting the uptake of neurotransmitters norepinephrine and serotonin by neurons. Flupentixol hydrochloride acts by blocking the dopamine (a neurotransmitter) receptors in brain cells. Excess amount of dopamine receptors normally act to modify behavior and overstimulation resulting in psychotic illness. Flupentixol blocks these receptors to control psychotic illness. Thus it is neuroleptic with anxiolytic and antidepressant properties. The combination of Flupentixol and Melitracen is indicated in the treatment of trigeminal neuralgia.

4. CLINICAL PARTICULARS OF FLUPENTIXOL-MELITRACEN

1.4.1 Pharmacological Properties

1.4.1.1 Pharmacodynamic property

The precise pharmacological mode of action of flupentixol-melitarcen has not been determined. It has been postulated that at low dosage flupentixol-melitracen binds to presynaptic dopamine receptors causing increased neurotransmitter release. There is evidence that postsynaptic aminergic receptors become down regulated in response to increased levels of neurotransmitter and this is responsible for the observed improvement in depressive symptoms. Flupentixol- Melitracen acts by blocking the dopamine (a neurotransmitter) receptors in the brain cells. Excess amount of dopamine receptors normally act to modify behavior and over-stimulation resulting in psychotic illness. Flupentixol- Melitracen blocks these receptors to control psychotic illness. Thus it is neuroleptic with anxiolytic and antidepressant properties.

1.4.1.2 Pharmacokinetic property

Mean oral bioavailability is about 55%. Maximum drug serum concentrations occur about 4 hours after dosing and the biological half-life is about 35 hours. Flupentixol- Melitracen is widely distributed in the body. Metabolism is by sulphoxidation, N-dealkylation and glucuronic acid conjugation. Excretion is via the urine and feces. Flupentixol- Melitracen has not

been studied in renal impairment. Increased cerebral sensitivity to antipsychotics has been noted in severe renal impairment. Flupentixol- Melitracen has not been studied in hepatic impairment. It is extensively metabolised by the liver and particular caution should be used in this situation and serum level monitoring is advised.

1.4.2 Indications

Anxiety, depression, apathy, Psychogenic depression, Depressive neuroses, Masked depression, Psychosomatic affections accompanied by anxiety and apathy, Menopausal depressions, Dysphoria and depression in alcoholics and drug addicts.

1.4.3 Posology & method of administration

Route of administration: Oral.

Adults-The standard initial dosage is 1 mg as a single morning dose. After one week the dose may be increased to 2 mg if there is inadequate clinical response. Daily dosage of more than 2 mg should be in divided doses up to a maximum of 3 mg daily.

Elderly-Elderly patients should receive half the recommended dosages. The standard initial dosage is 0.5 mg as a single morning dose. After one week, if response is inadequate, dosage may be increased to 1 mg once a day.Caution should be exercised in further increasing the dosage but occasional patients may require up to a maximum of 1.5 mg a day which should be given in divided doses.

Children-Not recommended for children.

1.4.4 Side effects

Undesirable effects are for the majority dose dependent. The frequency and severity are most pronounced in the early phase of treatment and decline during continued treatment.

Extrapyramidal reactions may occur, especially in the early phase of treatment. In most cases these side effects can be satisfactorily controlled by reduction of dosage and/or use of

antiparkinsonian drugs. The routine prophylactic use of antiparkinsonian drugs is not recommended.

Antiparkinsonian drugs do not alleviate tardive dyskinesia and may aggravate them. Reduction in dosage or, if possible, discontinuation of flupentixol- melitracen therapy is recommended. In persistent akathisia a benzodiazepine or propranolol may be useful.

Table 1.1: Side effects of Flupentixol-Melitracen

Cardiac disorders	Tachycardia, palpitations. Electrocardiogram QT prolonged.
Blood and lymphatic system disorders	Thrombocytopenia, neutropenia, leukopenia, agranulocytosis
Nervous system disorders	Somnolence, akathisia, hyperkinesia, hypokinesia. Tremor, dystonia, dizziness, headache, disturbance in attention. Tardive dyskinesia, dyskinesia, parkinsonism, speech disorder, convulsion. Neuroleptic malignant syndrome.
Eye disorders	Accommodation disorder, vision abnormal. Oculogyration.
Respiratory, thoracic andmediastinal disorders	Dyspnoea.
Gastrointestinal disorders	Dry mouth.

	Salivary hypersecretion, constipation, vomiting, dyspepsia, diarrhoea. Abdominal pain, nausea, flatulence.
Renal and urinary disorders	Micturition disorder, urinary retention.
Skin and subcutaneous tissuedisorders	Hyperhidrosis, pruritus. Rash, photosensitivity reaction, dermatitis.
Musculoskeletal and connective tissue disorder	Myalgia. Muscle rigidity.
Endocrine disorder	Hyperprolactinaemia.
Metabolism and nutrition disorders	Increased appetite, weight increased. Decreased appetite. Hyperglycaemia, glucose tolerance abnormal.
Vascular disorders	Hypotension, hot flush.
Immune system disorders	Hypersensitivity, anaphylactic reaction.
Hepatobiliary disorders	Liver function test abnormal. Jaundice
Reproductive system and breast disorders	Ejaculation failure, erectile dysfunction. Gynaecomastia, galactorrhoea, amenorrhoea.
Pregnancy, puerperium and perinatal conditions	Drug withdrawal syndrome neonatal
Psychiatric disorders	Insomnia, depression, nervousness, agitation,

	libido decreased. Confusional state.

1.4.5 Contraindications

The immediate recovery phase after myocardial infarction. Defects in bundle-branch conduction, untreated narrow angle glaucoma, acute alcohol, barbiturate and opiate intoxication. Flupentixol-Melitracen should not be given to patients who have received a MAO-inhibitor within two weeks. Not recommended for excitable or overactive patient since its activating effect may lead to exaggeration of these characteristics.

1.4.6 Drug Interaction

In common with other similar drugs, flupentixol- melitracen enhances the response to alcohol, the effects of barbiturates and other CNS depressants. Flupentixol-Melitracen may potentiate the effects of general anaesthetics and anticoagulants and prolong the action of neuromuscular blocking agents.The anticholinergic effects of atropine or other drugs with anticholinergic properties may be increased. Concomitant use of drugs such as metoclopramide, piperazine or antiparkinson drugs may increase the risk of extrapyramidal effects such as tardive dyskinesia. Combined use of antipsychotics and lithium or sibutramine has been associated with an increased risk of neurotoxicity.

Antipsychotics may enhance the cardiac depressant effects of quinidine; the absorption of corticosteroids and digoxin. The hypotensive effect of vasodilator antihypertensive agents such as hydralazine and α-blockers (e.g. doxazosin), or methyl-dopa may be enhanced.

Increases in the QT interval related to antipsychotic treatment may be exacerbated by the co-administration of other drugs known to significantly increase the QT interval. Co-administration of such drugs should be avoided. Drugs known to cause electrolyte disturbances such as thiazide diuretics (hypokalaemia) and drugs known to increase the plasma concentration

of flupentixol- melitracen should also be used with caution as they may increase the risk of QT prolongation and malignant arrythmias.

Antipsychotics may antagonise the effects of adrenaline and other sympathomimetic agents, and reverse the antihypertensive effects of guanethidine, possibly clonidine and similar adrenergic-blocking agents. Antipsychotics may also impair the effect of levodopa, adrenergic drugs and anticonvulsants.

1.4.7 In Pregnancy & Lactation

As the safety of flupentixol- melitracen in human pregnancy has not been established, use during pregnancy, especially the first and last trimesters, should be avoided, unless the expected benefit to the patient outweighs the potential risk to the foetus. The newborn of mothers treated with antipsychotics in late pregnancy, or labor, may show signs of intoxication such as lethargy, tremor and hyperexcitability, and have a low Apgar score. Neonates exposed to antipsychotics (including flupentixol) during the third trimester of pregnancy are at risk of adverse reactions including extrapyramidal and/or withdrawal symptoms that may vary in severity and duration following delivery. There have been reports of agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress, or feeding disorder. Consequently, newborns should be monitored carefully.

Flupentixol- Melitracen is excreted into the breast milk. If the use of Flupentixol-Melitracen is considered essential, nursing mothers should be advised to stop breast-feeding .

1.4.8 Precaution

Caution should be exercised in patients having: liver disease; cardiac disease or arrhythmias; 0severe respiratory disease; renal failure; epilepsy (and conditions predisposing to epilepsy e.g. alcohol withdrawal or brain damage); Parkinson’s disease; narrow angle glaucoma; prostatic hypertrophy; hypothyroidism; hyperthyroidism; myasthenia gravis; phaeochromocytoma and patients who have shown hypersensitivity to thioxanthenes or other antipsychotics.

If previously the patient has been treated with tranquilizers with sedative effects these should be withdrawn gradually. Use in Pregnancy and Lactation: Flupentixol - Melitracen should preferably not be given during pregnancy and lactation.

1.4.9 Overdose

Overdosage may cause somnolence, or even coma, extrapyramidal symptoms, convulsions, hypotension, shock, hyper-or hypothermia. ECG changes, QT prolongation, Torsade de Pointes, cardiac arrest and ventricular arrhythmias have been reported when administered in overdose together with drugs known to affect the heart (Medicines 2012).

Treatment is symptomatic and supportive, with measures aimed at supporting the respiratory and cardiovascular systems. The following specific measures may be employed if required.

• anticholinergic antiparkinson drugs if extrapyramidal symptoms occur.

• sedation (with benzodiazepines) in the unlikely event of agitation or excitement or convulsions.

• noradrenaline in saline intravenous drip if the patient is in shock. Adrenaline must not be given.

• Gastric lavage should be considered.

Chapter Two

Literature Review

LITERATURE REVIEW

Flupentixol (INN) is a typical antipsychotic drug of the thioxanthene class, it is also available as a combination product containing both melitracen and flupentixol.

Melitracen is a trycyclic antidepressant for the treatment of depression and anxiety.The pharmacology of melitracen has not been properly investigated and is largely unknown, but it act in a similar way to other TCAs. Indeed, melitracen is reported to have imipramine and amitriptyline-like effects.

In Bangladesh these flupentixol and melitracen drugs are available in a combination product marketed under brand name such as Adelax, Anzet, Tenexit, Anjenta, Fluxit etc. It has been reported recently that this combination drug (Flupentixol+Melitracen) is photosensitive. So, it means under light exposure (normal or extreme) the combination drug product degrades or may any of the active ingredient. But there is no published data regarding its photosensitivity. Flupentixol +Melitrcen, this combination product is packaged in transparent plastic blister. But, it is interesting that one pharmaceutical uses the opaque aluminum blister packaging system because of the photosensitive report. Since, there is no established data regarding photolytic degradation of flupentixol &melitracen combination product, we conducted a research program to determine whether this combination product is photosensitive or not. We hope that the consequence of this study will help us to extract the exact information about the photosensitivity which will bring a revolutionary change in the packaging system of the drug as well as the features of these drugs.

After the introduction of flupentixol and melitracen as a drug there were lot of research works took place regarding different parameters of this drug. But most of them are about the method development of chromatographic system.

Che et al.(che et al. 2007) developed an effective and productive method as well as validated, using Lequid Chromatography(LC)/Eletrospray Ionization (ESI)-Mass Spectroscopy(MS)/Mass Spectroscopy for simultaneous quantization of flupentixol(thioxanthene) and melitracen(TCA)—antidepressant drugs, in human plasma. The quantization of the target compounds was specified and determined in a multiple reaction monitoring (MRM) and positive ion mode (che et al. 2007) The method was effective and proved to be suitable for the study of bioequivalence research of antidepressant drug like flupentixol and melitacen in human plasma(che et al. 2007).

Earlier in 1999, Walter and his fellow research mates (Walter et al. 1999) developed a method for the quantification of both isomers of the thioxanthene neuroleptic flupentixol and of the butyrophenone derivative haloperidol in human serum, the method was a high-performance liquid chromatography (HPLC) which is a modern and most efficient form of liquid chromatography for its dynamic activity The suitability of the described method for therapeutic drug monitoring and clinical pharmacokinetic studies was assessed by analysis of more than 100 trough level serum samples(Walter et al 1999).

Again in 2006, another method was developed by a researcher group from Japan led by Tatsuo Shinozuka(Shinozuka et al. 2006), the method was Liquid chromatography/Mass spectroscopy with sonic ionization spray for the Solid-phase oriented extraction system and

involves analysis of numerous(amount was 20) antidepressant drugs including Flupentixol and Melitracen in human plasma(Shinozuka et al. 2006). These drugs showed good separation and sensitivity by LC–MS(Shinozuka et al. 2006). The present procedure exhibits an effective, easier and more convenient screening method for antidepressants thus it will be an useful for forensic toxicology investigations (Shinozuka et al. 2006).

But from this research group two researcher Tanaka and Terada(Tanaka et al. 1998) did a experiment in 1996 regarding forensic analysis of eleven cyclic antidepressants including our interest drug Melitracen in human biological samples. They developed a high-performance liquid chromatographic method for this experiment(Tanaka et al. 1998), they used reverse phase HPLC column for the experiment.

After that in 2000, Weinmann et al. (Weinmann et al. 2001) developed LC–MS–MS methods for the analysis of Neuroleptics in hair from Psychiatric Patients. The notable drugs in this experiment were Flupentixol, Haloperidol, Penfluridol, Clozapine etc.

Recently in India a researcher named B. Laxminarayana did a study on the development and validation of new analytical methods for the estimation of flupentixol dihydrochloride in bulk and pharmaceutical dosage form(Laxminarayana, 2011). Five simple, sensitive and specific methods have been developed for the quantitative estimation of Flupentixol dihydrochloride in bulk and pharmaceutical formulations which includes Zero, First, Second order derivative Spectroscopy, RP-HPLC and HPTLC(Laxminarayana, 2011).

In 2010 Chhalotiya et al. (Chhalotiya et al. 2011) did an research work on combination dosage form of antidepressant drug which contains Melitracen HCl and Flupentixol Dihydrochloride. The research was on development of liquid chromatography method for the

Simultaneous Determination of this combination preparation in the dosage form (Chhalotiya et al. 2011). It was a successful method in this research study which was executed for the assessment of combined dosage form. The proposed LC method can be enforced to the analysis of tablets collected during expedited stability experiments to assume expiration dates of pharmaceuticals product especially the combined products (Chhalotiya et al. 2011).

Another study was done by Yunus et al.(yunus et al. 2011) recently in 2011 which was determination of Flupentixol Dihydrochloride in bulk and Pharmaceutical product by using simple UV-spectroscopy method. The validity of the procedure described in study was assessed. Statistical analysis of the outcome has been carried out exhibit maximum accuracy and good precision. The proposed method was successfully implemented for the determination of flupenthixol dihydrochloride in pharmaceutical formulations without any undesired interaction from excipients(Yunus et al. 2011).

Again back in 2009 a reverse phase HPLC method has been developed by Sheikh et al(Sheikh et al. 2009) for estimation of Flupenthixol Hydrochloride in pharmaceutical dosage forms which is a simple, selective, rapid, precise and economical. The method proposed in the study can be used for determination and estimation flupentixol in combined dosage forms (Sheikh et al. 2009).

Different organic solvents like dimethyl formamide; acetonitrile, hexane, acetone, methanol, chloroform, alcohol, and carbon tetrachloride have been used for solubilization of poorly water soluble drugs for spectrophotometric estimations(M. C. Sharma et al. 2010). Backlash of organic solvents include excessive cost, toxicity and wrong analysis due to volatility.

In 2010 approaching to eradicate these backlashes, three new, simple, precise, environmental friendly, cost effective, safe, selective spectrophotometric methods have been developed by M. C. Sharma et al(M. C. Sharma et al. 2010). The primary goal of the present investigation was to employ these hydrotropic solutions to extract the drugs from their dosage forms, excluding the use of costlier organic solvents. Ultraviolet absorption spectrophotometric method for the estimation of poorly water soluble drugs like Melitracen HCl in pharmaceutical formulations has been developed(M. C. Sharma et al. 2010).

For development of the methods of quality control for TCA antidepressant and other CNS drug in pharmaceuticals Saldaña et al. (Saldaña et al. 2002) run a study which included micellar liquid chromatography methods. This method was for pharmaceutical preparations (capsules, pills, tablets, injections) containing tricyclic antidepressants amineptine, amitriptiline, clomipramine, doxepin, imipramine, melitracen and nortriptyline alone or together with other CNS drugs like diazepam, medazepam and perphenazine (Saldaña et al. 2002). Saldaña et al suggested that, Due to the versatility of interactions in micellar liquid chromatography, it is possible determine highly hydrophobic compounds such as TCAs in a short time using mobile phases containing low organic solvent concentrations and usual flow rates, in contrast with the RP-HPLC methods proposed for these compounds (Saldaña et al. 2002).

The next year Garcia et al. developed specific reversed phase-high pressure liquid chromatography (RP-HPLC) method for the simultaneous determination of flupenthixol (FPT) , clozapine (CZP), zuclopenthixol (ZPT) and loxapine (LXP), in human plasma(Garcia et al.2003). These antipsychotic drugs are frequently used for the management of schizophrenia and other neuropsychiatric diseases(Garcia et al.2003).This method is

isocratic as well as rapid which is useful for the management of acute intoxication(Garcia et al.2003).

In the year of 2007 Roman et al. used LC-MS-MS chromatographic process for the development of method for quantization of seven low-dosage antipsychotic drugs in human postmortem blood, the drugs are drugs buspirone, fluphenazine, flupenthixol, perphenazine, risperidone, ziprasidone, and zuclopenthixol(Roman et al 2007). Roman et al. stated that, in forensic toxicology, antipsychotic drugs are of considerable interest because of their abuse potential and their involvement in intoxications and suicides(Roman et al. 2007). The study reported that antipsychotic drugs should be considered not only in toxic concentrations but also in therapeutic levels in postmortem (Roman et al. 2007).

In recent days there were few reports founded regarding photosensitivity of flupentixol and melitracen drugs. Specifically the claim is against in combination product of these drugs. In 2010

Maquille et al. did a study about photolytic degradation flupentixol in aqueous solution under irradiation at 254 nm(Maquille et al. 2010). The structures of the photodegradation drugs were determined by ultra high performance liquid-chromatography linked to mass spectrometry after irradiation at 254 nm of aqueous solutions of the antipsychotic drug flupentixol(Maquille et al. 2010). From the experiment of Maquille et al. it was fond that, fragmentation patterns of the parent ions were established on a hybrid linear ion trap–orbitrap mass spectrometer allowing accurate mass measurements of both parent and daughter ions(Maquille et al. 2010). This permited to propose plausible structures for the main photolytic products of flupentixol. . A total of nine photoproducts were founded by the detector after irradiation of the drug. The main photoproduct is generated following the

addition of a hydroxyl group on the double bond adjacent to the thioxanthene ring (Maquille et al. 2010).

Chapter Three

MATERIALS & METHODS

3.1 MATERIALS

3.1.1 Sample Collection:

For the research purpose 500 tablets of Flupentixol-Melitracen (Flupentixol 0.5 mg & Melitracen 10 mg) a combined drug preparation (Brand Name-Anzet, manufactured by Popular Pharmaceutical) were collected from the local drug store in Dhaka as a sample. All samples are from same batch.

3.1.2 Samples

Table 3.1: Samples used in the experiment including source

Materials Name	Source (Supplier Name)
Anzet tablets	Popular Pharmaceutical Ltd.

3.1.3 Reagents

Table 3.2: Reagents used in the experiment including source

Reagents Name	Source (Supplier Name)
Concentrated Sulfuric acid	Germany
Distilled Water	Laboratory(East West University)

3.1.4 Equipments & Instruments

Table 3.3: Lists of equipments used for the experiment

Serial No.	Equipments	Source (Supplier Name)	Origin
1	Vernier Caliper	China Supplier	Shanghai,China
2	UV-Spectrophotometer	Shimadzu UV-1800	Japan
3	Distill Water Plant	SMIC	China

Serial No.	Equipments	Source (Supplier Name)	Origin
4	Electronic Balance	Precisa XB120A	Switzerland
5	Friability tester	Veegoindia	India
6	Hardness tester	Manually operated hardness tester	India

3.1.5 Images of Instruments

Figure 3.1: [Left to right] Vernier Caliper**,** Shimadzu UV-1800 Double Beam Spectrophotometer and Electronic Balance

Figure 3.2: [Left to right] Friability tester, Hardness Tester and Distilled water Plant

3.1.6 Apparatus

Following is the list of apparatus that we used throughout the experiment.

Table 3.4: List of Apparatus used throughout this project

Serial No.	Apparatus
1	Forceps
2	Funnel
3	Beakers
4	Spatula
5	Glass Rod
6	Filter Papers
7	Aluminum foil paper
8	Cling Wrap(Transparent plastic paper)
9	Plastic Containers
10	Mortar & Pastels
11	Test tubes
12	Volumetric Flasks (25ml,50 ml & 100 ml)
13	Pipette pumper
14	Pipette
15	Lamp
16	Thermometer
17	Bulb(25 & 40 Watt)

3.2 METHODS

3.2.1 Standard curve and equation derivation

The standard curve was prepared to compare the test result with it to determine the degradation of the drug. For standard curve preparation the average weight of 5 tablets were taken and all the 5 tablets was crashed by using mortar and pestle.The average weight of the 5 tablets which was previously measured was weight from thecrashed powder tablets. After measuring the powder drugs by the help of a balance, it was leftto dissolve in 100ml of 0.1N

H2SO4 solvent. Series of dilution was carried out with the standard stock solution by pipetting 2 ml of thestock solution in test tube (1) and adding 8 ml of solvent to it. Then again pipetting 2 ml solution from test tube (1) to test tube (2) and adding 8 ml solvent to it. This was continued for more 3 times. Thus producing a known concentration of Flupentixol dihydrochloride:

Table 3.5: Concentration of Flupentixol dihydrochloride

Serial No.	Concentration (mg)
1	0.01
2	0.002
3	0.0004
4	0.00008
5	0.000016

Following is the Concentration of Melitracen hydrochloride

Table 3.6: Concentration of Melitracen hydrochloride

Serial No.	Concentration (mg)
1	0.2
2	0.04
3	0.008
4	0.0016
5	0.00032

Absorbance of the above solutions were taken to 229 nm wavelength for Flupentixol dihydrochloride and 258 nm wavelength for Melitracen hydrochloride in UVSpectrophotometer and the observed value was plotted against concentration and a linearregression equation was obtained.

3.2.2 Samples Under Exposure to Light

To determine the photo stability of the drug the tablets were subjected to various types of photo exposure, which are:

- Electric Bulb exposure (25 watt, 40 watt)
- Sunlight exposure(summer)
- Exposure to normal room temperature (14 days, 28 days, 35 days, 45 days)

3.2.2.1 Electric Bulb exposure (25 watt, 40 watt)

Two power ranges of bulb, 25 watt and 40 watt were used as the artificial light source. Thirty tablets were kept on a solid surface and were placed under 25 watt containing lamp. A thermometer was kept behind the tablets submerge in a glass of water to measure the temperature. We kept the tablets for nine hour and after each three hour 10 tablet were collected. In three hour 10 tablets where collected as 3 hour exposed sample and with more 3 hour the 6 hour exposed sample and finally with addition of more 3 hour the 9 hour sample was collected. After the sample collection analysis of the sample was conducted by measuring some physical parameters and UV visible spectroscopy to determine the potency of the drug.

3.2.2.2 Sunlight exposure

For Sunlight exposed sample the tablets were exposed to the summer sun. Thirty tablets were kept on a paper with a thermometer for the sun exposure. In three hour 10 tablets where collected as 3 hour exposed sample and with more 3 hour the 6 hour exposed sample and finally with addition of more 3 hour the 9 hour sample was collected. Each sample containing 10 tablets.

3.2.2.3 Exposure to normal room temperature

The exposure of the tablets was done in normal room temperature. Hundred tablets were kept in the normal room temperature in a plastic transparent container. We rapped the container with transparent plastic paper(cling wrap) so that moisture and air cannot enter to the container. We started the preservation of the tablets in the box on 23rd February 2012.

We fixed our observation date after 14 days, 35days, 49 days and each time we took out 10 tablets from the container. After the sample collection analysis of the sample was conducted by measuring some physical parameters and UV visible spectroscopy to determine the potency of the drug.

3.2.2.4 Sample analysis

After the collection of the sample it was time to proceed to the analysis step. At first the average weight of the three sample tablets were taken by the electronic balance. Then the tablets were crashed to fine powder by the help of mortar and pestle. The average weight that was previously accounted was then weighted from the crashed powdered sample and was allowed to dissolve into 100ml of 0.1N H_2SO_4 in a 100 ml volumetric flask. The solution of the volumetric flask was then filtered thought a filter paper.10 ml of the filtrate was pipette to a 100ml volumetric flask and 0.1 N H_2SO_4 was then added up to 100 ml.

After all that, the sample solution was prepared for the potency test using UV-Spectroscopy. For that, each of the tests was run against a blank, and for the test the test solution was poured into the quartz cell. The quartz cell was then placed into the holder situated inside the machine. Using a specified software technology the absorbance of the sample solution was established in the computer.

3.2.3 Physical parameters determination

3.2.3.1Weight Variation Test

Weight variation test is most significant because it has a relationship with content uniformity of a solid dosage forms. Any of the following factors, can produce excessive tablet variations:

1. Poor granulation flow properties, resulting in uneven die fill.
2. A wide variation in granulation particle size, which result in a variation in die fill density as a function of particle size and particle size distribution at different points in the production run.

3.2.3.1.1 Procedure

1. 10 tablets were taken and weighed all the tablets.
2. The average was taken and it was considered as the standard weight of an individual tablet.
3. All the tablets were weighed individually and observed whether the individual tablets are within the range or not.

The variation from the average weight in the weights not more than two tablets must not

differ more than the percentage listed below:

Table 3.7: Accepted percentage list for the weight variation test of tablets

Weight of tablet	Percentage difference
130 mg or less	±10%
More than 130 to 324 mg	±7.5%
More than 324 mg	±5%

3.2.3.1.2 Calculation

We used following equation to determined % Weight Variation of tablets

% Weight Variation = (A~I/I) ×100.

Where,

Initial Weight of Tablet, I (gm)

Average weight of Tablet, A (gm)

3.2.3.2 Thickness test

The thickness test was carried out to measure the thickness of the sample tablet, to determine the deviation of the tablet thickness due to the exposure of the light. It was done by using a Vernier caliper.

3.2.3.2.1 Procedure

1. First placing the tablet between the two jaws of the Vernier caliper.
2. Then, the main scale reading was taken.
3. The Vernier scale was taken also.
4. The two reading was added together by multiplying with the Vernier constant.

3.2.3.2.2 Calculation

We used following formula to determined thickness of the tablets.

Thickness of the table = reading of cm scale + reading of Vernier scale + Vernier error

3.2.3.3 Hardness Test of Tablets

Tablet hardness is usually expressed as the load required crushing a tablet placed on its edge. Hardness is thus sometimes termed the tablet crushing strength. The suitability of a tablet in regard to mechanical stability during packaging and shipment can usually be predicted on the basis of hardness. Tablet hardness, in turn, influences tablet density and porosity. It may affect tablet friability and disintegration time. It usually affects drug dissolution and release and it may affect bioavailability.

3.2.3.3.1 Procedure

1. The slide scale of the hardness tester was made zero
2. One tablet was placed vertically between two jaws.
3. Force was applied with a screw thread and spring until the tablet fractured.
4. Reading in Kg was taken from the sliding scale.

3.2.3.4 Friability Test of Tablets

Friction and shock are the forces that most often cause tablets to chip, cap or break. The friability test is closely related to tablet hardness and is designed to evaluate the ability of the tablet to withstand abrasion in packaging, handling and shipping. The value is expressed as a percentage.

3.2.3.4.1 Procedure

1. 10 tablets were weighted. It was considered as an initial reading
2. The tablet were placed in the section 1 of the drum of the friability tester and rotated 100 times.
3. The tablets were re-weighted. It was considered as a final reading.
4. The percent loss was calculated.
5. According to the U.S.P the tablets should not lose more than 1% of their total weight

3.2.3.4.2 Calculation:

We used following formula to determined Friability of the tablets

% weight loss = (Initial weight – Final weight) ÷Initial weight × 100%

Chapter Four

RSULT & DISCUSSION

4.1 RESULTS

4.1.1 Standard curve preparation

We found different absorption for different concentration of Flupentixol dihydrochloride on the tablet solution following is a table of those concentration and absorbance.

Table 4.1: Concentration and Absorbance for Standard Curve of Flupentixol dihydrochloride

Concentration(mg/ml)	Absorbance
0.01	1.094
0.002	0.221
0.0004	0.041
0.00008	0.033
0.000016	0.01

By plotting the concentration against the absorbance of Flupentixol dihydrochloride we founda straight line. From the Standard Curve of Flupentixol dihydrochloride we derived the equation Y=108.3X+0.008 and R2=0.999. We use this equation to get the concentration from different samples absorbance of Flupentixol dihydrochloride.

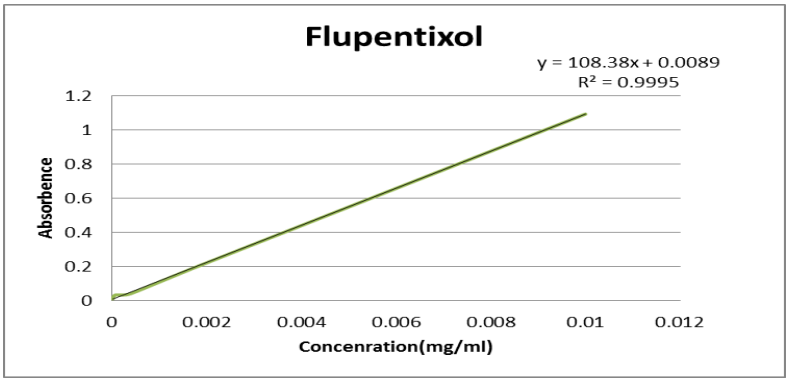

Figure 4.1: Plot showing straight line for Absorbance with respect to Concentration for Flupentixol

We found different absorption for different concentration of Melitracen hydrochloride on the tablet solution following is a table of those concentration and absorbance.

Table 4.2: Concentration and Absorbance for Standard Curve of Melitracen hydrochloride

Concentration(mg/ml)	Absorbance
0.2	0.97
0.04	0.201
0.008	0.043
0.0016	0.01
0.00032	0.044

By plotting the concentration against the absorbance of Melitracen hydrochloride we found a straight line. From the Standard Curve of Melitracen hydrochloride we derived the equation Y=4.765X+0.015 and R2=0.998. We use this equation to get the concentration from different samples absorbance of Melitracen hydrochloride.

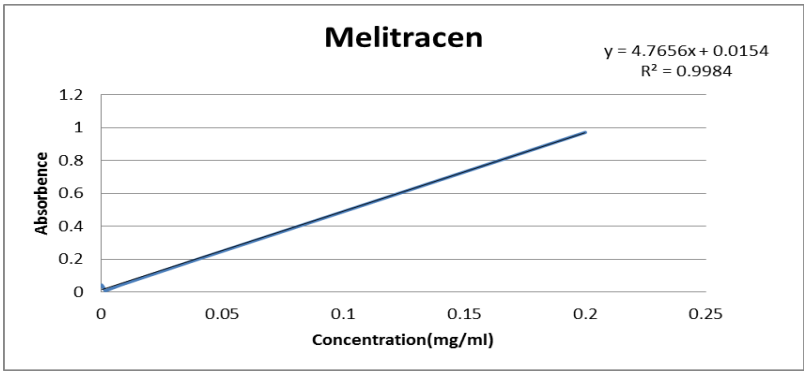

Figure 4.2: Plot showing straight line for Absorbance with respect to Concentration for Melitracen

4.1.2 Result of Samples Exposed Under 25 Watt Light

4.1.2.1 Samples Exposed to Light for 3 Hours

10 sample tablets were exposed to 25 watt light source for 3 hours. After 3 hours samples were collected. Then different physical parameter tests were conducted. Data of these tests are given bellow.

4.1.2.1.1 Data of Weight variation test (3 hours)

Table 4.3: Weight Variation test of the sample, Exposed to light for 3 hours

Tablet no.	Initial Weight, I(gm)	Average weight A(gm)	% Weight Variation; (A~I/I)×100
1	0.1048		-1.908
2	0.0996		3.2
3	0.1059		-2.927
4	0.1017		1.081
5	0.1039	0.1028	-1.05
6	0.1021		0.685
7	0.1023		0.488
8	0.1007		2.085
9	0.1050		-2.095
10	0.0973		5.6

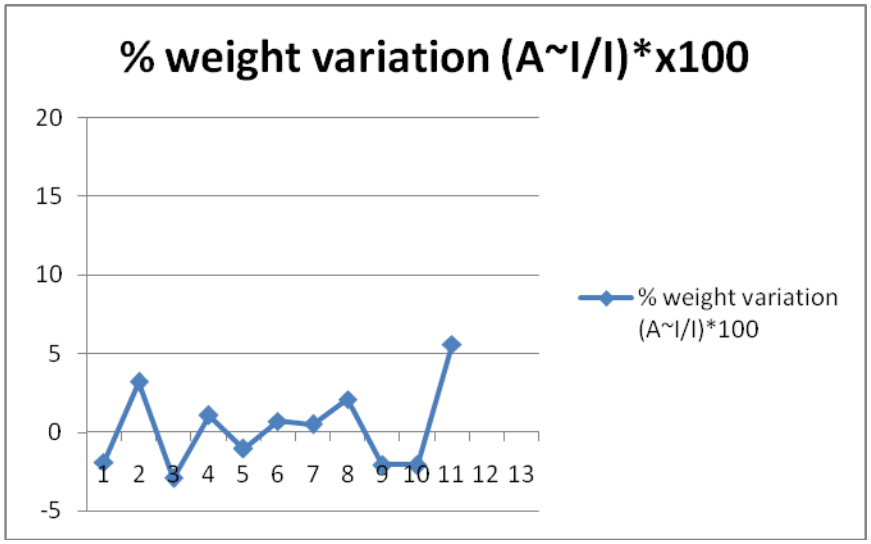

Figure 4.3: Scattered Plot showing weight variation of samples (exposed to light for 3 hours)

4.1.2.1.2 Data Thickness Test (3 hours)

Table 4.4: Thickness test of the sample, Exposed to light for 3 hours

Tablet no.	Main scale reading(cm), M	Vernier scale reading(cm), V	Thickness of the tablets (cm), i.e.(M+V) cm
1	0.4	0.09	0.49
2	0.4	0.09	0.49
3	0.4	0.09	0.49
4	0.4	0.095	0.495
5	0.4	0.09	0.49
6	0.4	0.095	0.495
7	0.4	0.095	0.495
8	0.4	0.095	0.495
9	0.4	0.09	0.49
10	0.4	0.09	0.49

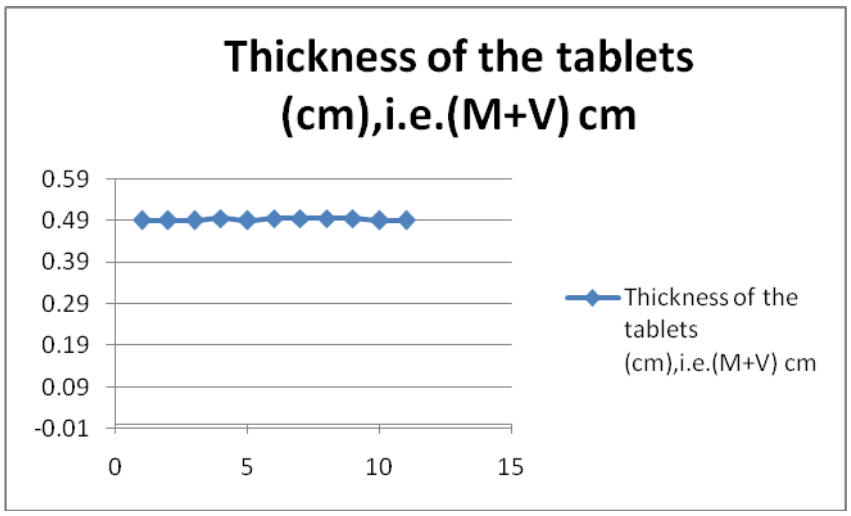

Figure 4.4: Scattered Plot showing thickness of samples (exposed to light for 3 hours)

4.1.2.1.3 Data of Hardness test (3 hours)

Table 4.5: Hardness test of the sample, Exposed to light for 3 hours

Tablet no.	Hardness(kg)	Hardness Average (kg)
1	2	1.9
2	1.9	1.9
3	2	1.9

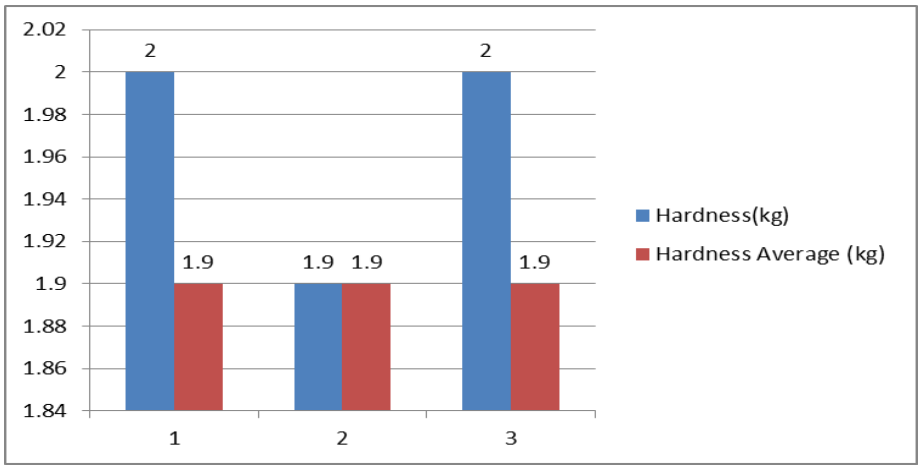

Figure 4.5: Column showing the difference of Hardness (kg) with Hardness Average (kg) of tablets (exposed to light for 3 hours).

4.1.2.1.4 Data of Friability test (3 hours)

Table 4.6: Friability test of the sample, Exposed to light for 3 hours

Initial weight	Weight after rotation	Friability
1. 028	1. 026	0.19%

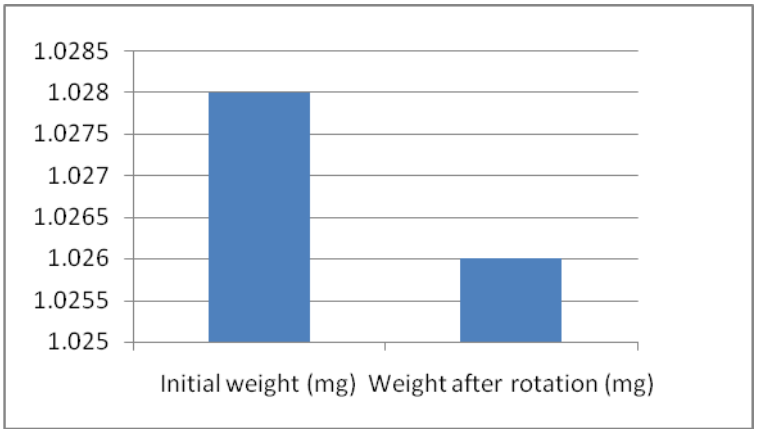

Figure 4.6: Column showing the difference of Initial weight (gm) with Weight after rotation (gm) of tablets (exposed to light for 3 hours).

4.1.2.2 Samples Exposed to Light for 6 Hours

10 sample tablets were exposed to 25 watt light source for 6 hours. After 6 hours samples were collected. Then different physical parameter tests were conducted. Data of these tests are given bellow.

4.1.2.2.1 Data of Weight variation test (6 hours)

Table 4.7: Weight Variation test of the sample, Exposed to light for 6 hours

Tablet no.	Initial Weight, I(gm)	Average weight A(gm)	% Weight Variation; (A~I/I)×100
1	0.1031		-1.55
2	0.1012	0.1015	0.3
3	0.1009		0.59

Tablet no.	Initial Weight, I(gm)	Average weight A(gm)	% Weight Variation; (A~I/I)×100
5	0.1004		1.9
6	0.1035		-1.93
7	0.1038	0.1015	-2.21
8	0.1034		-1.84
9	0.0988		2.73
10	0.0986		2.94

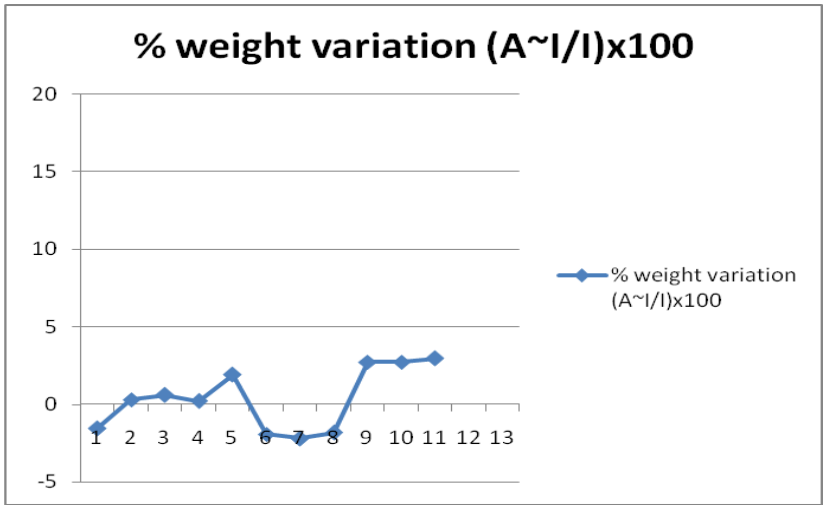

Figure 4.7: Scattered Plot showing weight variation of samples (exposed to light for 6 hours)

4.1.2.2.2 Data Thickness Test (6 hours)

Table 4.8: Thickness test of the sample, Exposed to light for 6 hours

Tablet no.	Main scale reading(cm), M	Vernier scale reading(cm), V	Thickness of the tablets (cm), i.e.(M+V) cm
1	0.375	0.06	0.44
2	0.375	0.06	0.44
3	0.375	0.065	0.44
4	0.375	0.07	0.45
5	0.375	0.06	0.44
6	0.375	0.07	0.45
7	0.375	0.065	0.44
8	0.375	0.07	0.45
9	0.375	0.07	0.45
10	0.375	0.07	0.45

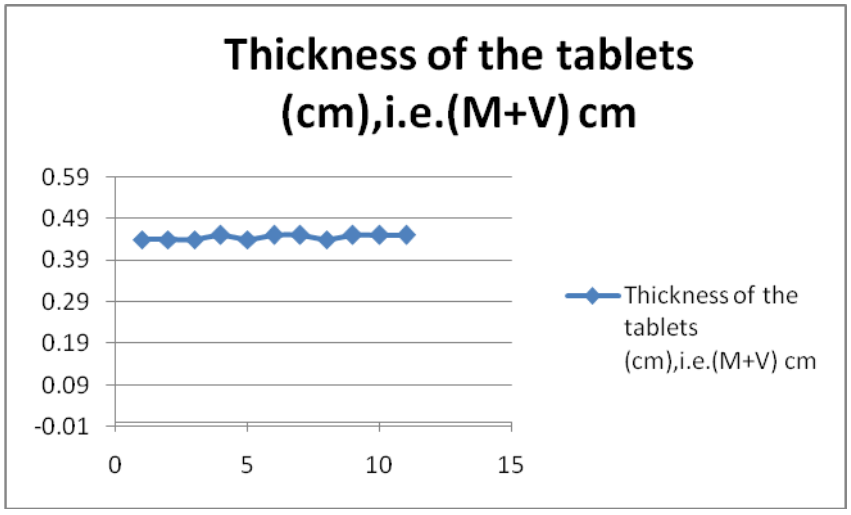

Figure 4.8: Scattered Plot showing thickness of samples (exposed to light for 6 hours)

4.1.2.2.3 Data of Hardness test (6 hours)

Table 4.9: Hardness test of the sample, Exposed to light for 6 hours

Tablet no.	Hardness(kg)	Hardness Average (kg)
1	2.1	1.9
2	1.9	1.9
3	1.8	1.9

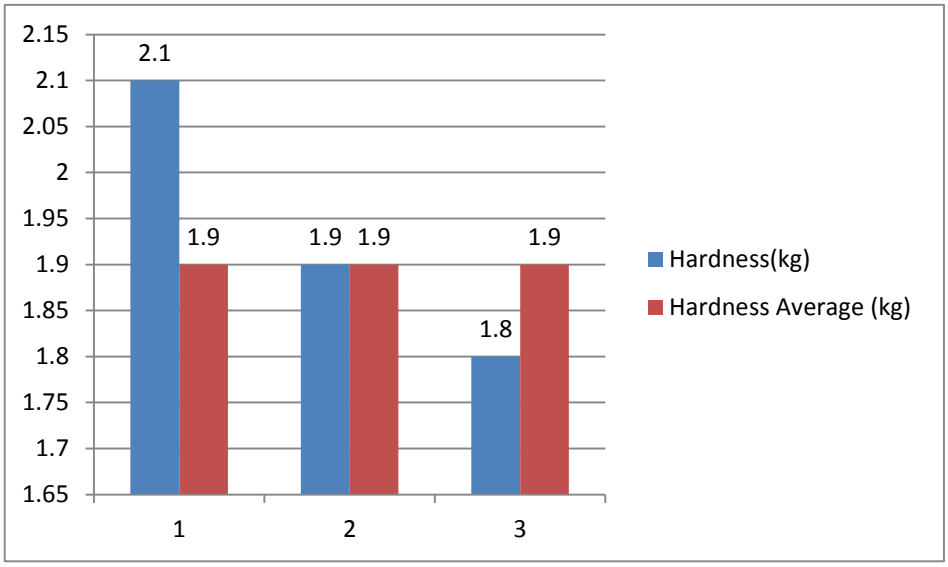

Figure 4.9: Column showing the difference of Hardness (kg) with Hardness Average (kg) of tablets (exposed to light for 6 hours).

4.1.2.2.4 Data of Friability test (6 hours)

Table 4.10: Friability test of the sample, Exposed to light for 6 hours

Initial weight	Weight after rotation	Friability
1.015	1.013	0.19%

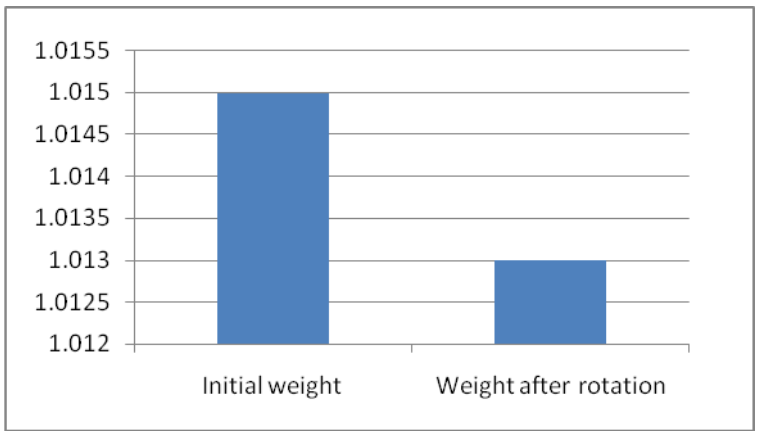

Figure 4.10: Column showing the difference of Initial weight (gm) with Weight after rotation (gm) of tablets (exposed to light for 6 hours).

4.1.2.3 Samples Exposed to Light for 9 Hours

10 sample tablets were exposed to 25 watt light source for 9 hours. After 9 hours samples were collected. Then different physical parameter tests were conducted. Data of these tests are given bellow.

4.1.2.3.1 Data of Weight variation test (9 hours)

Table 4.11: Weight Variation test of the sample, Exposed to light for 9 hours

Tablet no.	Initial Weight, I(gm)	Average weight A(gm)	% Weight Variation; (A~I/I)×100
1	0. 0983		3.85
2	0.1090		-6.3
3	0.1023		-0.19
4	0.1007		1.3
5	0.1018	0.1021	0.29
6	0.1029		-0.77
7	0.0992		0.29

Tablet no.	Initial Weight, I(gm)	Average weight A(gm)	% Weight Variation; (A~I/I)×100
9	0.1075	0.1021	-5.02
10	0.1027		-0.58

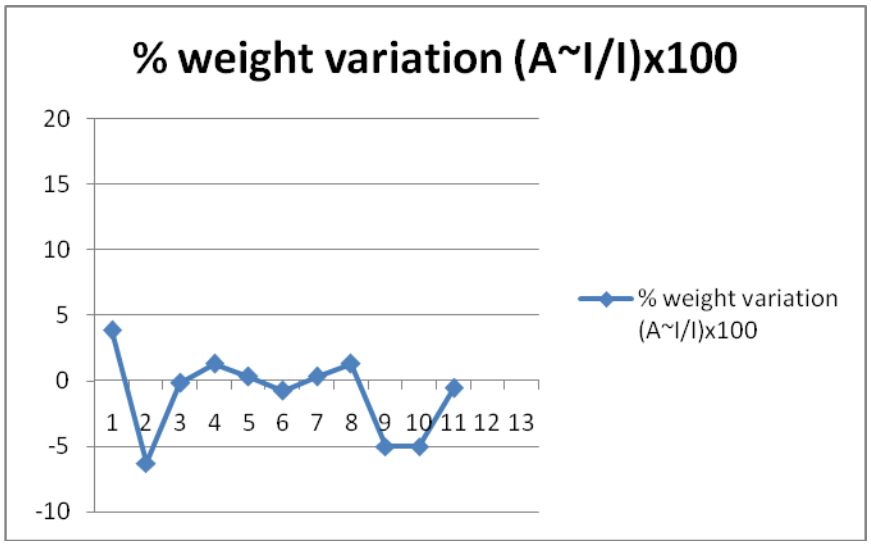

Figure 4.11: Scattered Plot showing weight variation of samples (exposed to light for 9 hours)

4.1.2.3.2 Data Thickness Test (9 hours)

Table 4.12: Thickness test of the sample, Exposed to light for 9 hours

Tablet no.	Main scale reading(cm), M	Vernier scale reading(cm), V	Thickness of the tablets (cm), i.e.(M+V) cm
1	0.4	0.09	0.49
2	0.4	0.09	0.49
3	0.4	0.09	0.49
4	0.4	0.095	0.495
5	0.4	0.09	0.49
6	0.4	0.095	0.495

Tablet no.	Main scale reading(cm), M	Vernier scale reading(cm), V	Thickness of the tablets (cm), i.e.(M+V) cm
8	0.4	0.095	0.495
9	0.4	0.09	0.49
10	0.4	0.09	0.49

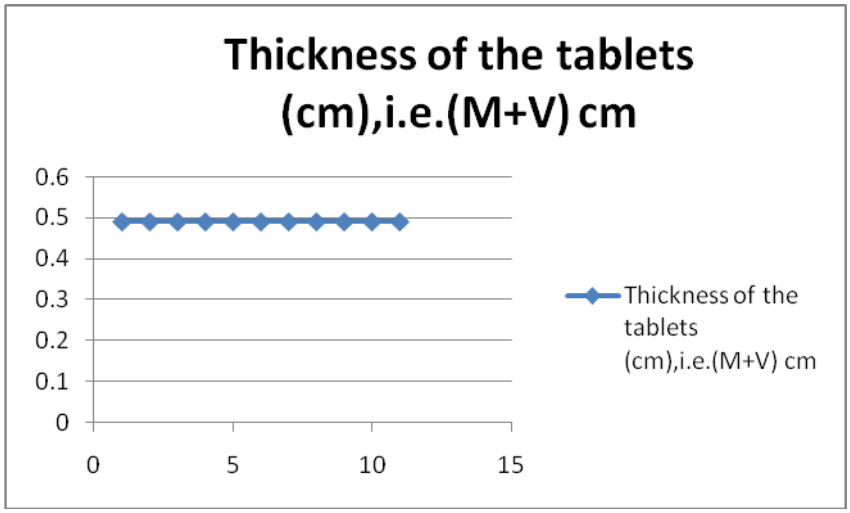

Figure 4.12: Scattered Plot showing thickness of samples (exposed to light for 9 hours)

4.1.2.3.3 Data of Hardness test (9 hours)

Table 4.13: Hardness test of the sample, Exposed to light for 9 hours

Tablet no.	Hardness(kg)	Hardness Average (kg)
1	2.4	2.4
2	2.6	2.4
3	2.2	2.4

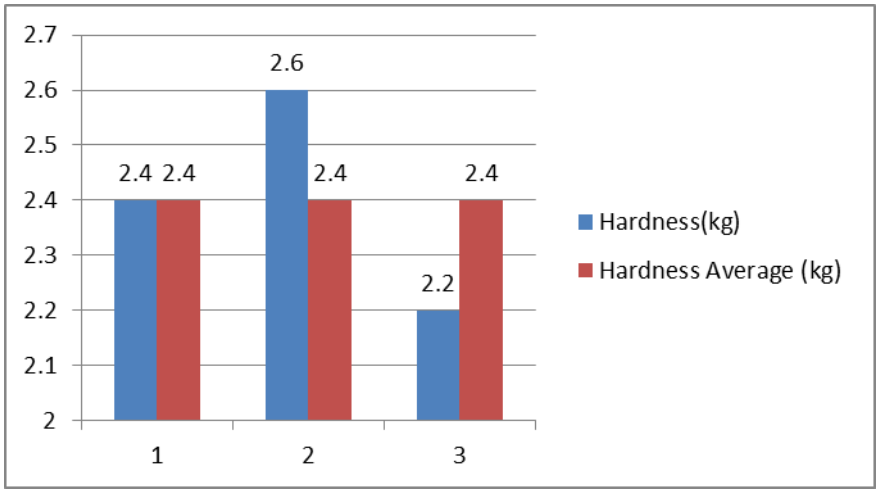

Figure 4.13: Column showing the difference of Hardness (kg) with Hardness Average (kg) of tablets (exposed to light for 9 hours).

4.1.2.3.4 Data of Friability test (9 hours)

Table 4.14: Friability test of the sample, Exposed to light for 9 hours

Initial weight	Weight after rotation	Friability
1. 021	1.018	0.29%

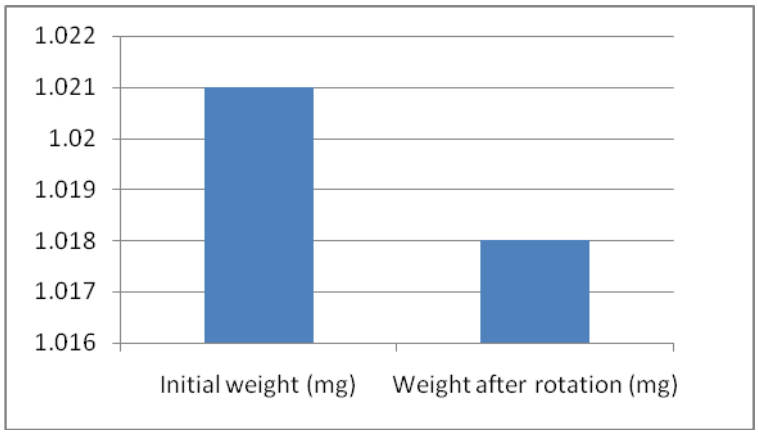

Figure 4.14: Column showing the difference of Initial weight (gm) with Weight after rotation (gm) of tablets (exposed to light for 9 hours).

4.1.3 Result of Samples Exposed Under 40 Watt Light

4.1.3.1 Samples Exposed to Light for 3 Hours

10 sample tablets were exposed to 40 watt light source for 3 hours. After 3 hours samples were collected. Then different physical parameter tests were conducted. Data of these tests are given bellow.

4.1.3.1.1 Data of Weight variation test (3 hours)

Table 4.15: Weight Variation test of the sample, Exposed to light for 3 hours

Tablet no.	Initial Weight, I(gm)	Average weight A(gm)	% Weight Variation; (A~I/I)×100
1	0.0986		2.73
2	0.1036		-0.23
3	0.1009		0.04
4	0.102		-0.07
5	0.1004	0.1013	0.09
6	0.1029		-0.16
7	0.1004		0.09
8	0.1022		-0.09
9	0.103		-0.17
10	0.1038		-0.25

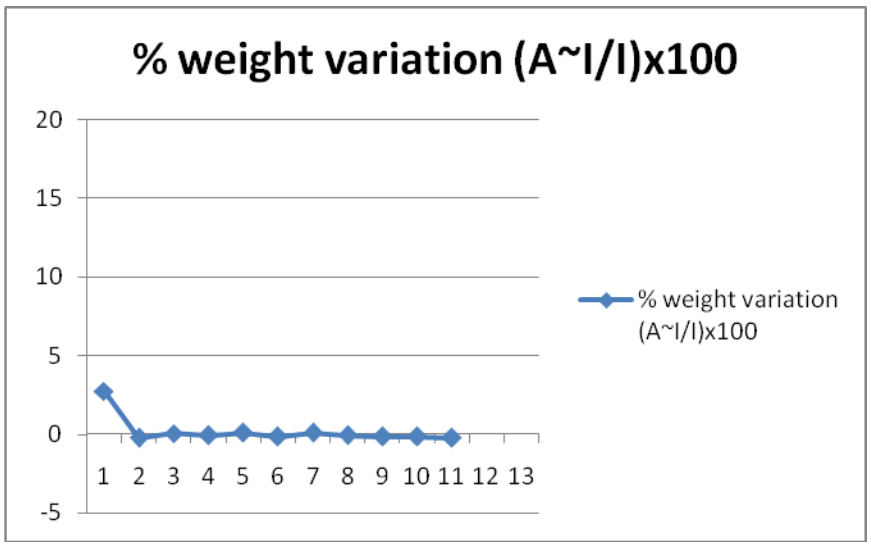

Figure 4.15: Scattered Plot showing weight variation of samples (exposed to light for 3 hours)

4.1.3.1.2 Data Thickness Test (3 hours)

Table 4.16: Thickness test of the sample, Exposed to light for 3 hours

Tablet no.	Main scale reading(cm), M	Vernier scale reading(cm), V	Thickness of the tablets (cm), i.e.(M+V) cm
1	0.4	0.09	0.49
2	0.4	0.09	0.49
3	0.4	0.09	0.49
4	0.4	0.095	0.495
5	0.4	0.09	0.49
6	0.4	0.095	0.495
7	0.4	0.095	0.495
8	0.4	0.095	0.495
9	0.4	0.09	0.49
10	0.4	0.09	0.49

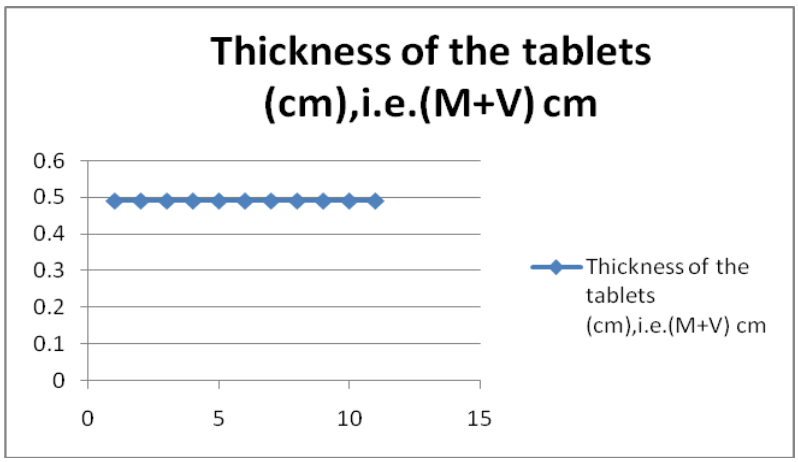

Figure 4.16: Scattered Plot showing thickness of samples (exposed to light for 3 hours)

4.1.3.1.3 Data of Hardness test (3 hours)

Table 4.17: Hardness test of the sample, Exposed to light for 3 hours

Tablet no.	Hardness(kg)	Hardness Average (kg)
1	1.8	1.9
2	2.1	1.9
3	1.8	1.9

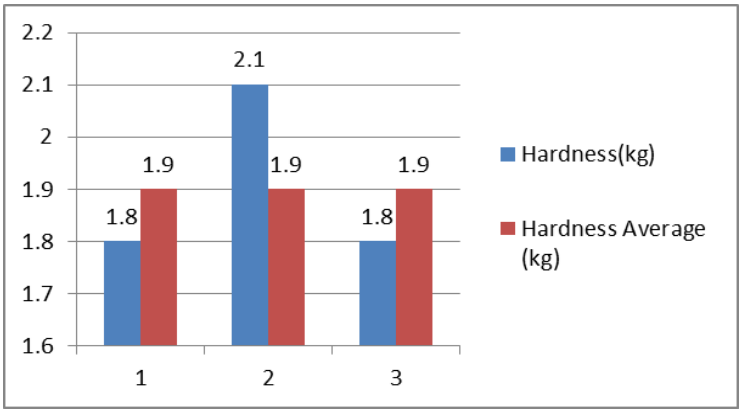

Figure 4.17: Column showing the difference of Hardness (kg) with Hardness Average (kg) of tablets (exposed to light for 3 hours).

4.1.3.1.4 Data of Friability test (3 hours)

Table 4.18: Friability test of the sample, Exposed to light for 3 hours

Initial weight	Weight after rotation	Friability
1. 0134	1.0132	0.02%

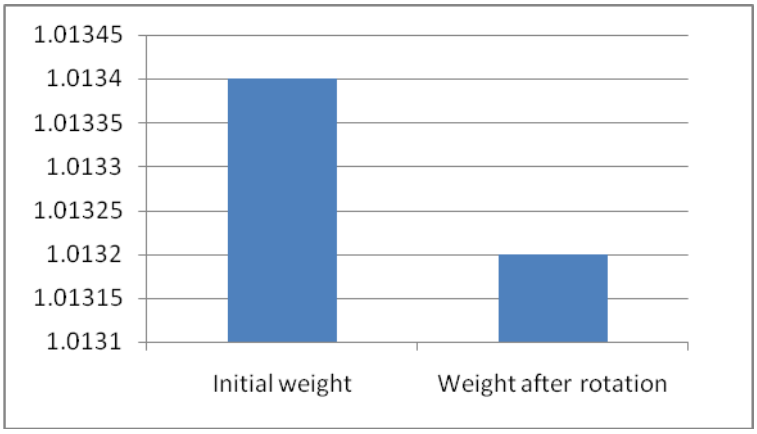

Figure 4.18: Column showing the difference of Initial weight (gm) with Weight after rotation (gm) of tablets (exposed to light for 3 hours).

4.1.3.2 Samples Exposed to Light for 6 Hours

10 sample tablets were exposed to 40 watt light source for 6 hours. After 6 hours samples were collected. Then different physical parameter tests were conducted. Data of these tests are given bellow.

4.1.3.2.1 Data of Weight variation test (6 hours)

Table 4.19: Weight Variation test of the sample, Exposed to light for 6 hours

Tablet no.	Initial Weight, I(gm)	Average weight A(gm)	% Weight Variation; (A~I/I)×100
1	0.1008		0.89
2	0.1046		-2.77
3	0.0995		2.21
4	0.1001		1.5
5	0.107	0.1017	-4.9
6	0.1012		0.05
7	0.1007		0.99
8	0.1028		-1.07
9	0.0993		2.417
10	0.1022		-0.48

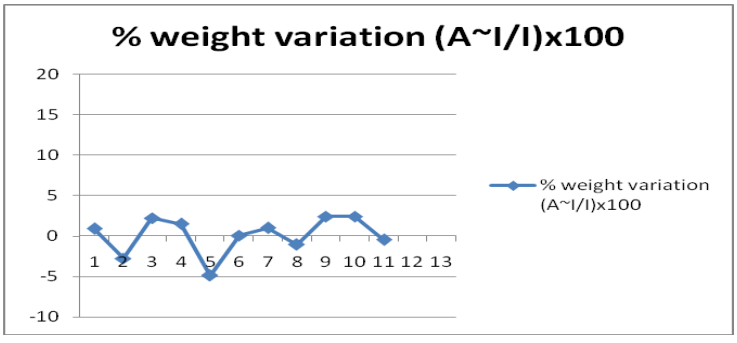

Figure 4.19: Scattered Plot showing weight variation of samples (exposed to light for 6 hours)

4.1.3.2.2 Data Thickness Test (6 hours)

Table 4.20: Thickness test of the sample, Exposed to light for 6 hours

Tablet no.	Main scale reading(cm), M	Vernier scale reading(cm), V	Thickness of the tablets (cm), i.e.(M+V) cm
1	0.4	0.09	0.49
2	0.4	0.09	0.49
3	0.4	0.09	0.49
4	0.4	0.095	0.495
5	0.4	0.09	0.49
6	0.4	0.095	0.495
7	0.4	0.095	0.495
8	0.4	0.095	0.495
9	0.4	0.09	0.49
10	0.4	0.09	0.49

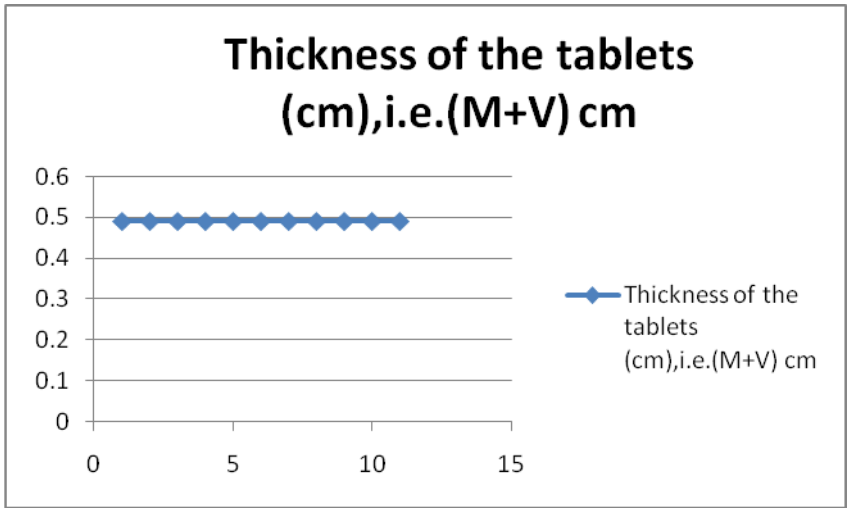

Figure 4.20: Scattered Plot showing thickness of samples (exposed to light for 6 hours)

4.1.3.2.3 Data of Hardness test (6 hours)

Table 4.21: Hardness test of the sample, Exposed to light for 6 hours

Tablet no.	Hardness(kg)	Hardness Average (kg)
1	2.1	2.06
2	2.1	2.06
3	2	2.06

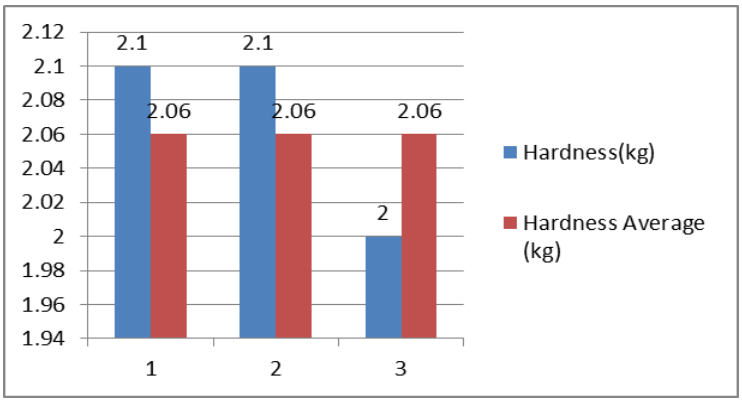

Figure 4.21: Column showing the difference of Hardness (kg) with Hardness Average (kg) of tablets (exposed to light for 6 hours).

4.1.3.2.4 Data of Friability test (6 hours)

Table 4.22: Friability test of the sample, Exposed to light for 6 hours

Initial weight	Weight after rotation	Friability
1. 0171	1.0166	0.05%

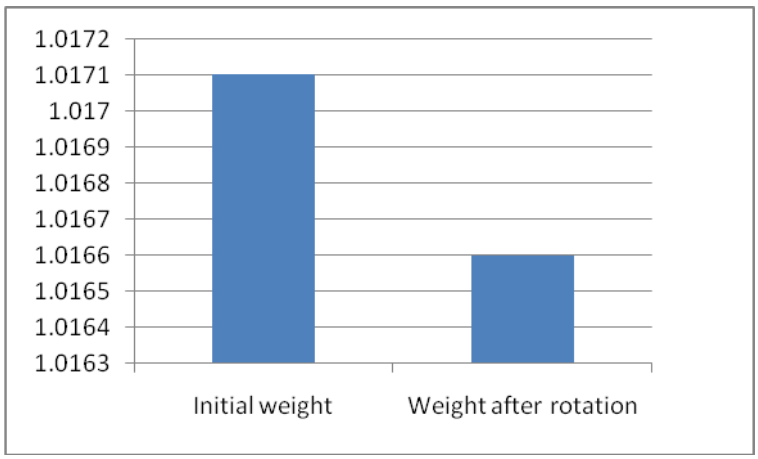

Figure 4.22: Column showing the difference of Initial weight (gm) with Weight after rotation (gm) of tablets (exposed to light for 6 hours).

4.1.3.3 Samples Exposed to Light for 9 Hours

10 sample tablets were exposed to 40 watt light source for 9 hours. After 9 hours samples were collected. Then different physical parameter tests were conducted. Data of these tests are given bellow.

4.1.3.3.1 Data of Weight variation test (9 hours)

Table 4.23: Weight Variation test of the sample, Exposed to light for 9 hours

Tablet no.	Initial Weight, I(gm)	Average weight A(gm)	% Weight Variation; (A~I/I)×100
1	0.1032		-0.67
2	0.0993		3.22
3	0.106	0.1025	-3.3
4	0.1035		-0.966
5	0.0988		3.7
6	0.1045		-1.91

Tablet no.	Initial Weight, I(gm)	Average weight A(gm)	% Weight Variation; (A~I/I)×100
8	0.1025		0
9	0.1036	0.1025	-1.06
10	0.1012		1.2

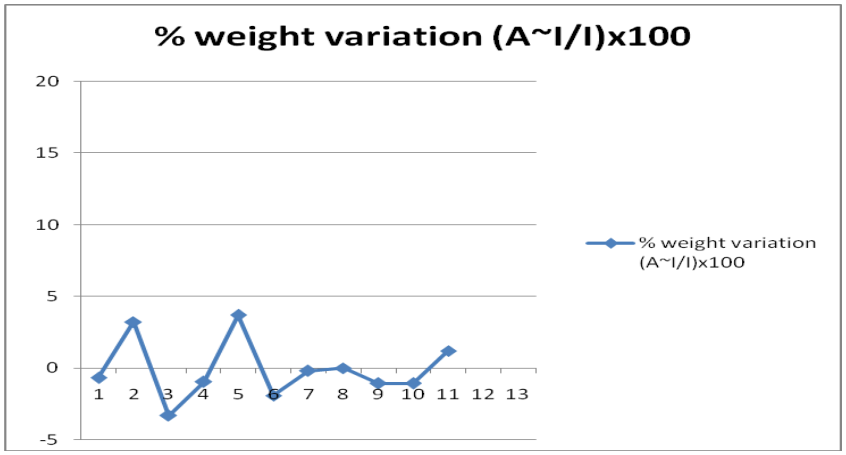

Figure 4.23: Scattered Plot showing weight variation of samples (exposed to light for 9 hours)

4.1.3.3.2 Data Thickness Test (9 hours)

Table 4.24: Thickness test of the sample, Exposed to light for 9 hours

Tablet no.	Main scale reading(cm), M	Vernier scale reading(cm), V	Thickness of the tablets (cm), i.e.(M+V) cm
1	0.4	0.09	0.49
2	0.4	0.09	0.49
3	0.4	0.09	0.49
4	0.4	0.095	0.495
5	0.4	0.09	0.49

Tablet no.	Main scale reading(cm), M	Vernier scale reading(cm), V	Thickness of the tablets (cm), i.e.(M+V) cm
6	0.4	0.095	0.495
7	0.4	0.095	0.495
8	0.4	0.095	0.495
9	0.4	0.09	0.49
10	0.4	0.09	0.49

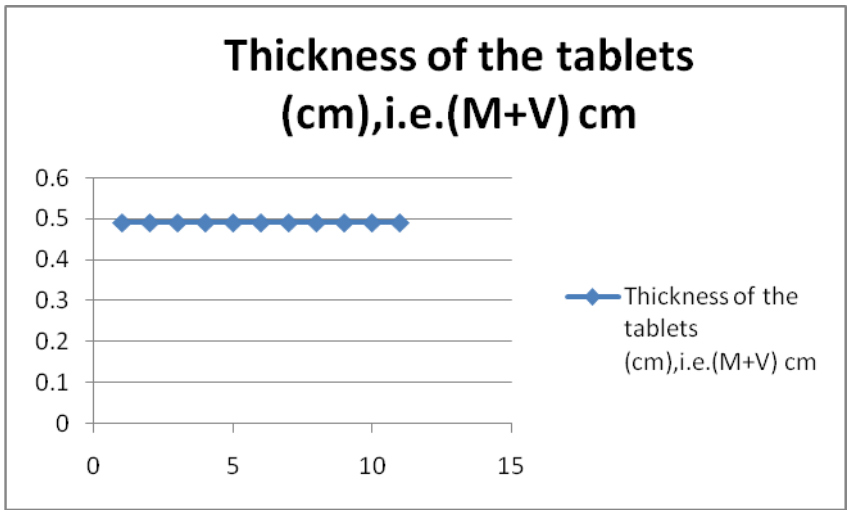

Figure 4.24: Scattered Plot showing thickness of samples (exposed to light for 9 hours)

4.1.3.3.3 Data of Hardness test (9 hours)

Table 4.25: Hardness test of the sample, Exposed to light for 9 hours

Tablet no.	Hardness(kg)	Hardness Average (kg)
1	2.6	2.4
2	2.4	2.4
3	2.2	2.4

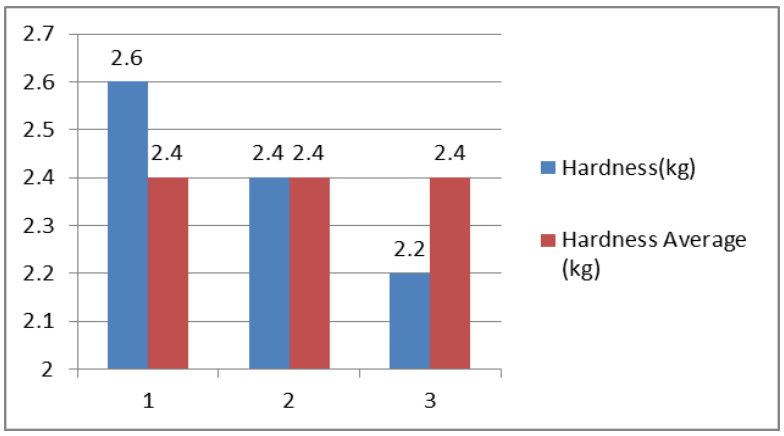

Figure 4.25: Column showing the difference of Hardness (kg) with Hardness Average (kg) of tablets (exposed to light for 9 hours).

4.1.3.3.4 Data of Friability test (9 hours)

Table 4.26: Friability test of the sample, Exposed to light for 9 hours

Initial weight	Weight after rotation	Friability
1. 0253	1.0245	0.08%

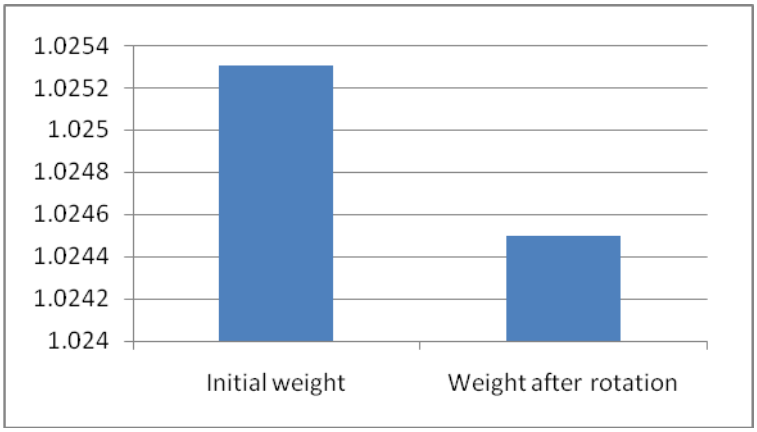

Figure 4.26: Column showing the difference of Initial weight (gm) with Weight after rotation (gm) of tablets (exposed to light for 9 hours).

4.1.4 Result of Samples Exposed Under Sunlight Light

4.1.4.1 Samples Exposed to Sunlight for 3 Hours

10 sample tablets were exposed to sunlight source for 3 hours. After 3 hours samples were collected. Then different physical parameter tests were conducted. Data of these tests are given bellow.

4.1.4.1.1 Data of Weight variation test (3 hours)

Table 4.27: Weight Variation test of the sample, Exposed to Sunlight for 3 hours

Tablet no.	Initial Weight, I(gm)	Average weight A(gm)	% Weight Variation; (A~I/I)×100
1	0.1025		-0.29
2	0.1033		-1.06
3	0.1039		-1.63
4	0.1		2.2
5	0.1022	0.1022	0
6	0.1018		0.39
8	0.1013		-0.09
9	0.1013	0.1022	-0.09
10	0.104		-1.73

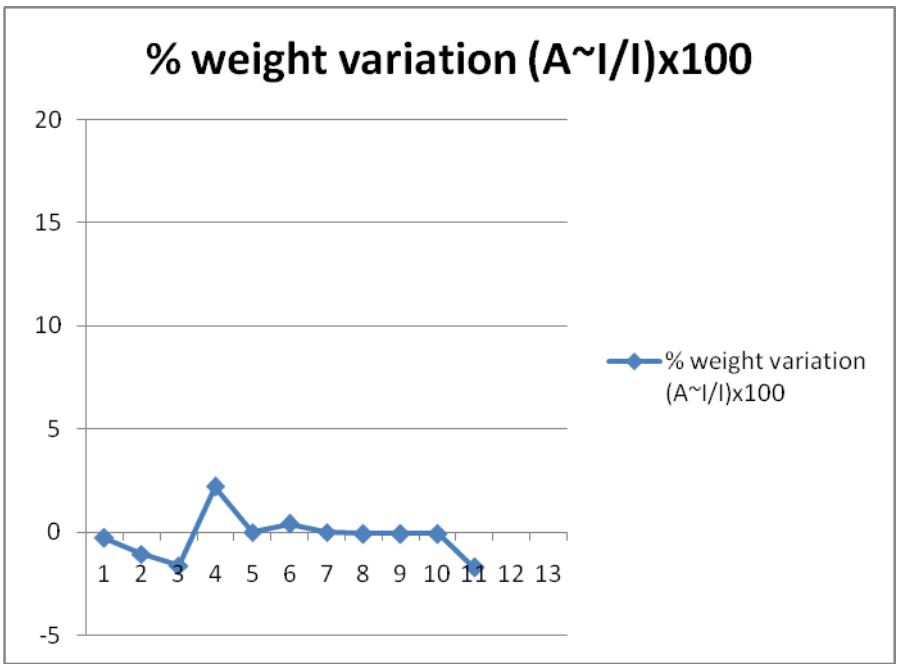

Figure 4.27: Scattered Plot showing weight variation of samples (exposed to sunlight for 3 hours)

4.1.4.1.2 Data Thickness Test (3 hours)

Table 4.28: Thickness test of the sample, Exposed to sunlight for 3 hours

Tablet no.	Main scale reading(cm), M	Vernier scale reading(cm), V	Thickness of the tablets (cm), i.e.(M+V) cm
1	0.4	0.07	0.47
2	0.4	0.07	0.47
3	0.4	0.07	0.47
4	0.4	0.07	0.47
5	0.4	0.07	0.47
6	0.4	0.07	0.47
7	0.4	0.07	0.47

Tablet no.	Main scale reading(cm), M	Vernier scale reading(cm), V	Thickness of the tablets (cm), i.e.(M+V) cm
8	0.4	0.07	0.47
9	0.4	0.07	0.49
10	0.4	0.07	0.49

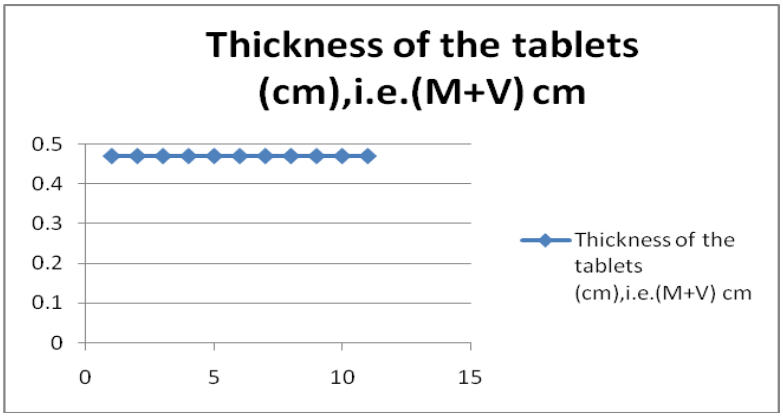

Figure 4.28: Scattered Plot showing thickness of samples (exposed to sunlight for 3 hours)

4.1.4.1.3 Data of Hardness test (3 hours)

Table 4.29: Hardness test of the sample, Exposed to sunlight for 3 hours

Tablet no.	Hardness(kg)	Hardness Average (kg)
1	2.2	2.03
2	2	2.03
3	1.9	2.03

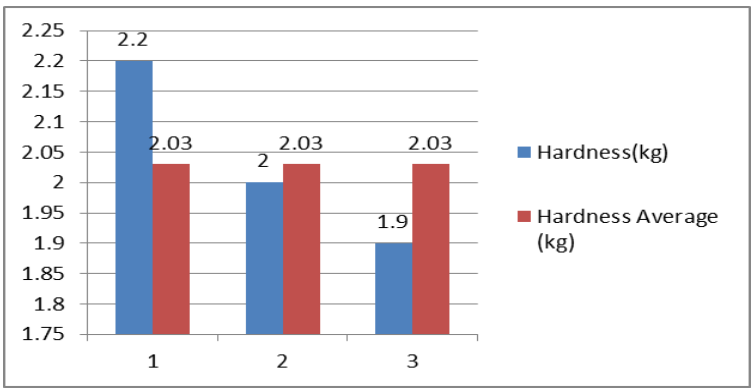

Figure 4.29: Column showing the difference of Hardness (kg) with Hardness Average (kg) of tablets (exposed to sunlight for 3 hours).

4.1.4.1.4 Data of Friability test (3 hours)

Table 4.30: Friability test of the sample, Exposed to sunlight for 3 hours

Initial weight	Weight after rotation	Friability
1. 0226	1.0220	0.026%

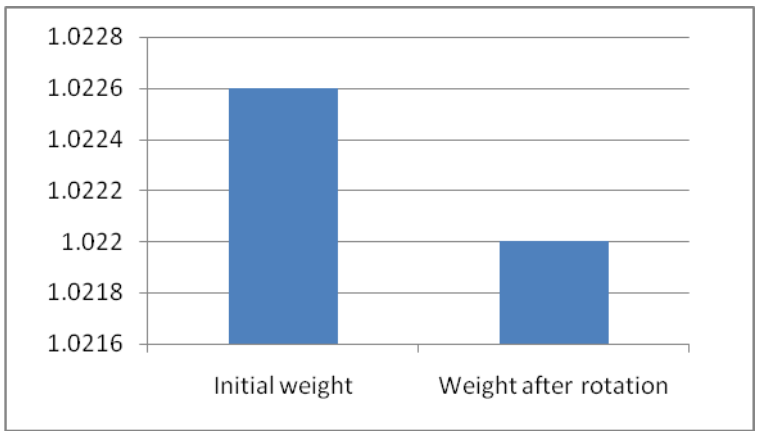

Figure 4.30: Column showing the difference of Initial weight (gm) with Weight after rotation (gm) of tablets (exposed to sunlight for 3 hours).

4.1.4.2 Samples Exposed to Sunlight for 6 Hours

10 sample tablets were exposed to sunlight source for 6 hours. After 6 hours samples were collected. Then different physical parameter tests were conducted. Data of these tests are given bellow.

4.1.4.2.1 Data of Weight variation test (6 hours)

Table 4.31: Weight Variation test of the sample, Exposed to sunlight for 6 hours

Tablet no.	Initial Weight, I(gm)	Average weight A(gm)	% Weight Variation; (A~I/I)×100
1	0.1023		-0.01
2	0.0992		2
3	0.1026		-0.14
4	0.1006		0.5
5	0.1018	0.1012	-0.06
6	0.1023		-0.11
7	0.1027		-0.15
8	0.1056		-0.44
9	0.1019	0.1012	-0.68
10	0.0995		1.7

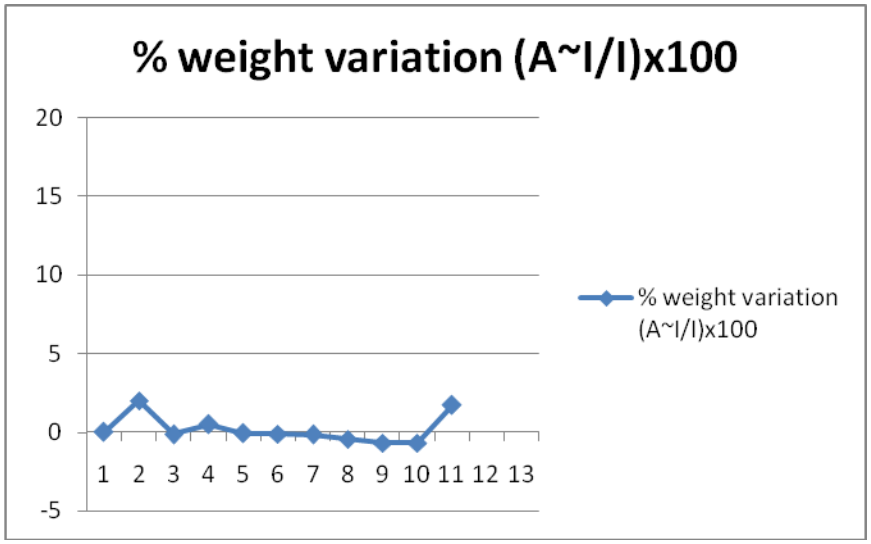

Figure 4.31: Scattered Plot showing weight variation of samples (exposed to sunlight for 6 hours)

4.1.4.2.2 Data Thickness Test (6 hours)

Table 4.32: Thickness test of the sample, Exposed to sunlight for 6 hours

Tablet no.	Main scale reading(cm), M	Vernier scale reading(cm), V	Thickness of the tablets (cm), i.e.(M+V) cm
1	0.4	0.09	0.49
2	0.4	0.09	0.49
3	0.4	0.09	0.49
4	0.4	0.095	0.495
5	0.4	0.09	0.49
6	0.4	0.095	0.495
7	0.4	0.095	0.495
8	0.4	0.095	0.495
9	0.4	0.09	0.49
10	0.4	0.09	0.49

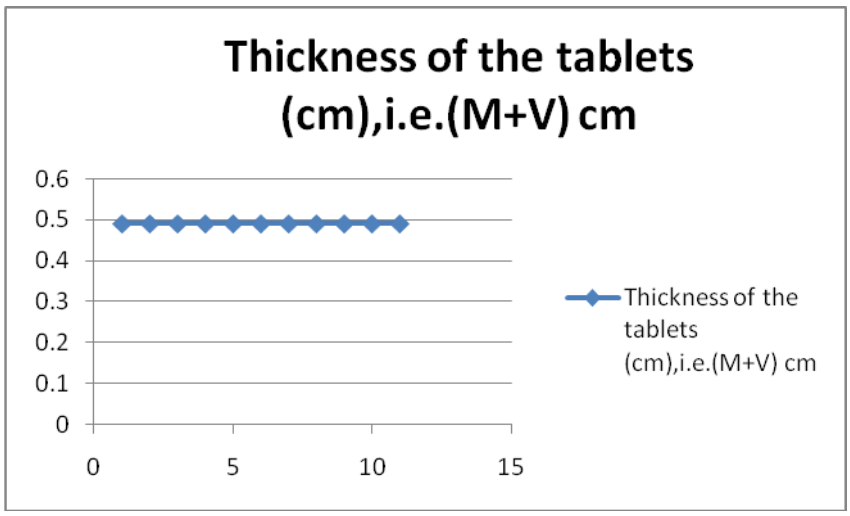

Figure 4.32: Scattered Plot showing thickness of samples (exposed to sunlight for 6 hours)

4.1.4.2.3 Data of Hardness test (6 hours)

Table 4.33: Hardness test of the sample, Exposed to sunlight for 6 hours

Tablet no.	Hardness(kg)	Hardness Average (kg)
1	1.6	1.6
2	1.5	1.6
3	1.7	1.6

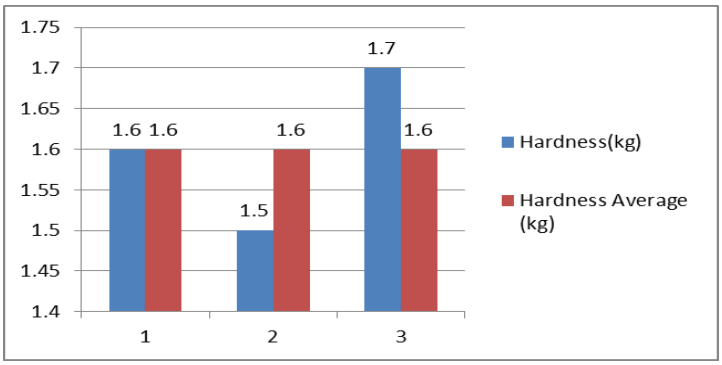

Figure 4.33: Column showing the difference of Hardness (kg) with Hardness Average (kg) of tablets (exposed to sunlight for 6 hours).

4.1.4.2.4 Data of Friability test (6 hours)

Table 4.34.1: Friability test of the sample, Exposed to sunlight for 6 hours

Initial weight	Weight after rotation	Friability
1. 0121	1.0118	0.03%

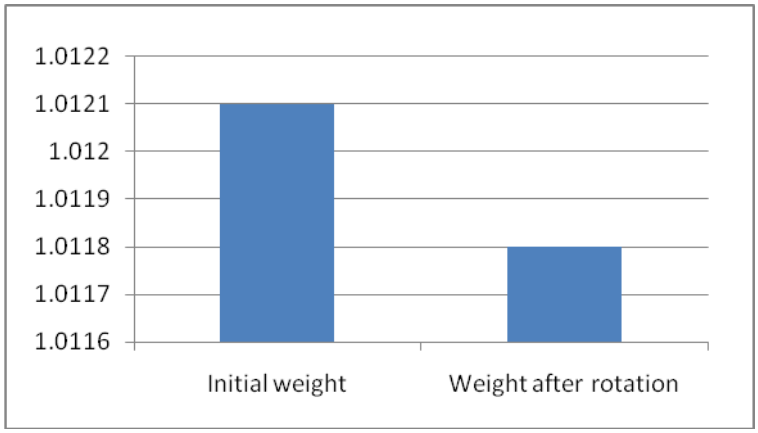

Figure 4.34.1: Column showing the difference of Initial weight (gm) with Weight after rotation (gm) of tablets (exposed to sunlight for 6 hours).

4.1.4.3 Samples Exposed to Sunlight for 9 Hours

10 sample tablets were exposed to sunlight source for 9 hours. After 9 hours samples were collected. Then different physical parameter tests were conducted. Data of these tests are given bellow.

4.1.4.3.1 Data of Weight variation test (9 hours)

Table 4.34.2: Weight Variation test of the sample, Exposed to sunlight for 9 hours

Tablet no.	Initial Weight, I(gm)	Average weight A(gm)	% Weight Variation; (A~I/I)×100
1	0.1005	0.1012	0.69
2	0.0997		1.5

Tablet no.	Initial Weight, I(gm)	Average weight A(gm)	% Weight Variation; (A~I/I)×100
3	0.1028		-1.55
4	0.1014		-0.19
5	0.1006	0.1012	0.59
6	0.1015		-0.29
7	0.0983		2.95
8	0.1029		-1.65
9	0.1015		-0.295
10	0.1027		-1.46

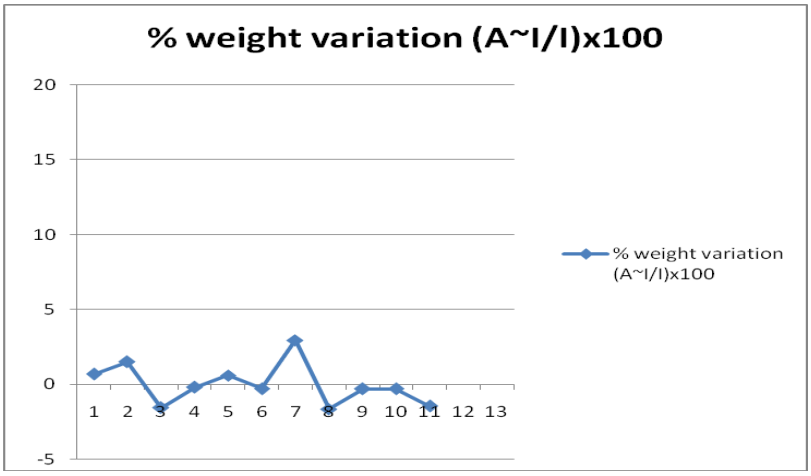

Figure 4.34.2: Scattered Plot showing weight variation of samples (exposed to sunlight for 9 hours)

4.1.4.3.2 Data Thickness Test (9 hours)

Table 4.35: Thickness test of the sample, Exposed to sunlight for 9 hours

Tablet no.	Main scale reading(cm), M	Vernier scale reading(cm), V	Thickness of the tablets (cm), i.e.(M+V) cm
1	0.4	0.09	0.49
2	0.4	0.09	0.49
3	0.4	0.09	0.49
4	0.4	0.095	0.495
5	0.4	0.09	0.49
6	0.4	0.095	0.495
7	0.4	0.095	0.495
8	0.4	0.095	0.495
9	0.4	0.09	0.49
10	0.4	0.09	0.49

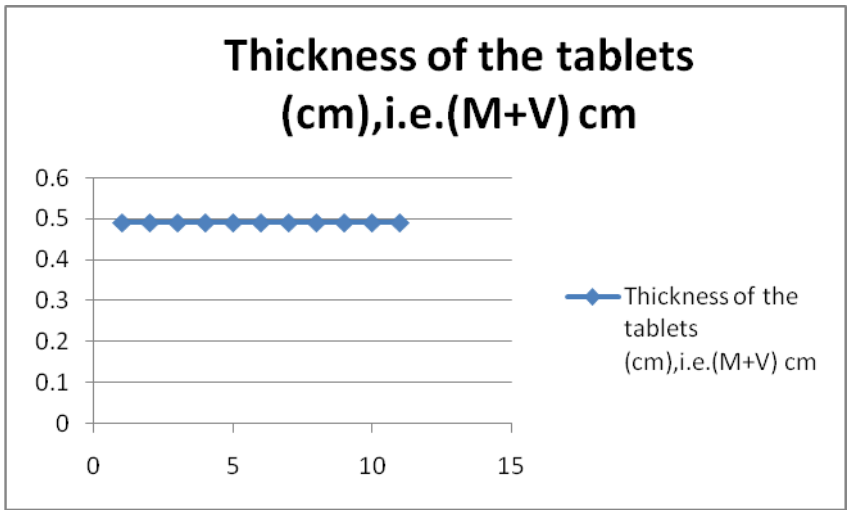

Figure 4.35: Scattered Plot showing thickness of samples (exposed to sunlight for 9 hours)

4.1.4.3.3 Data of Hardness test (9 hours)

Table 4.36: Hardness test of the sample, Exposed to sunlight for 9 hours

Tablet no.	Hardness(kg)	Hardness Average (kg)
1	1.8	1.73
2	1.8	1.73
3	1.6	1.73

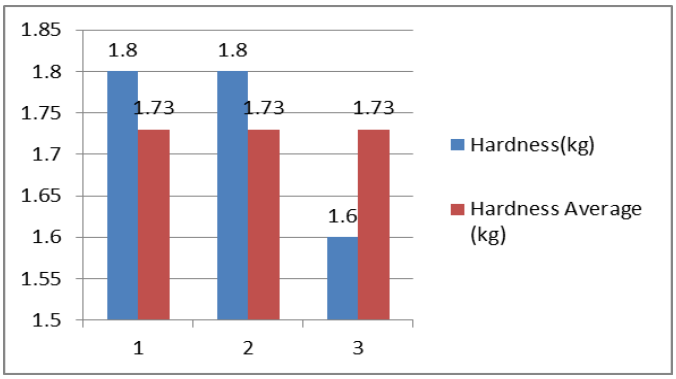

Figure 4.36: Column showing the difference of Hardness (kg) with Hardness Average (kg) of tablets (exposed to sunlight for 9 hours).

4.1.4.3.4 Data of Friability test (9 hours)

Table 4.37: Friability test of the sample, Exposed to sunlight for 9 hours

Initial weight	Weight after rotation	Friability
1. 0119	1.0116	0.029%

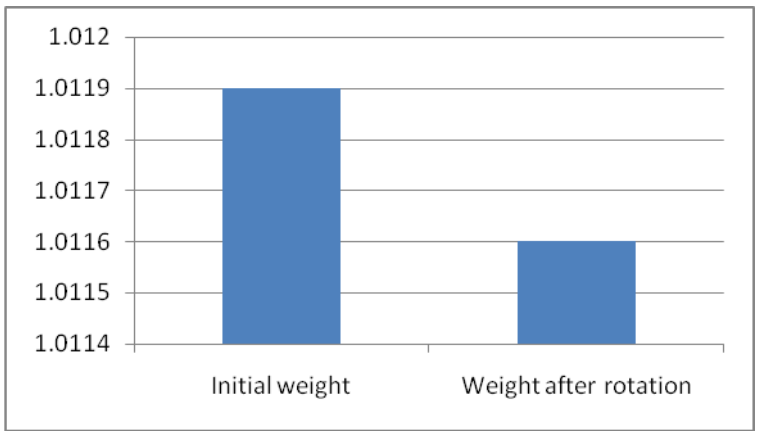

Figure 4.37: Column showing the difference of Initial weight (gm) with Weight after rotation (gm) of tablets (exposed to sunlight for 9 hours).

4.1.5 Result of Samples Exposed Under Normal Lightening Condition

4.1.5.1 Samples Exposed to Normal Light for 14 Days

10 sample tablets were exposed to normal light source for 14 days. After 14 days samples were collected. Then different physical parameter tests were conducted. Data of these tests are given bellow.

4.1.5.1.1 Data of Weight variation test

Table 4.38: Weight Variation test of the sample, Exposed to normal light for 14 days

Tablet no.	Initial Weight, I(gm)	Average weight A(gm)	% Weight Variation; (A~I/I)×100
1	0.1032		-0.67
2	0.0993		3.22
3	0.106	0.1025	-3.3
4	0.1035		-0.966
5	0.0988		3.7

Tablet no.	Initial Weight, I(gm)	Average weight A(gm)	% Weight Variation; (A~I/I)×100
6	0.1045		-1.91
7	0.1027		-0.19
8	0.1025	0.1025	0
9	0.1036		-1.06
10	0.1012		1.2

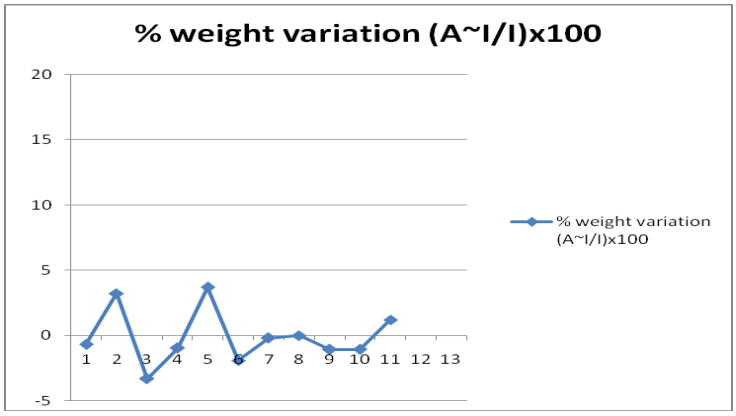

Figure 4.38: Scattered Plot showing weight variation of samples (exposed to normal light for 14 days)

4.1.5.1.2 Data Thickness Test

Table 4.39: Thickness test of the sample, Exposed to normal light for 14 days

Tablet no.	Main scale reading(cm), M	Vernier scale reading(cm), V	Thickness of the tablets (cm), i.e.(M+V) cm
1	0.4	0.085	0.485
2	0.4	0.085	0.485
3	0.4	0.085	0.485

Tablet no.	Main scale reading(cm), M	Vernier scale reading(cm), V	Thickness of the tablets (cm), i.e.(M+V) cm
4	0.4	0.085	0.485
5	0.4	0.085	0.485
6	0.4	0.085	0.485
7	0.4	0.085	0.485
8	0.4	0.085	0.485
9	0.4	0.085	0.485
10	0.4	0.085	0.485

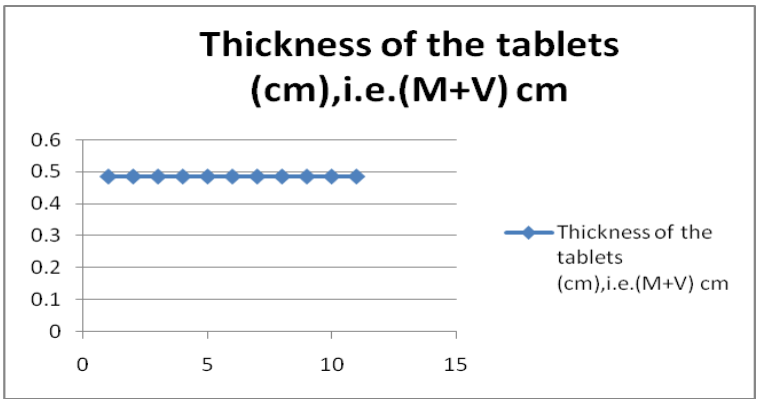

Figure 4.39: Scattered Plot showing thickness of samples (exposed to normal light for14 days)

4.1.5.1.3 Data of Hardness test

Table 4.40: Hardness test of the sample, Exposed to normal light for 14 days

Tablet no.	Hardness(kg)	Hardness Average (kg)
1	2.6	2.4
2	2.4	2.4
3	2.2	2.4

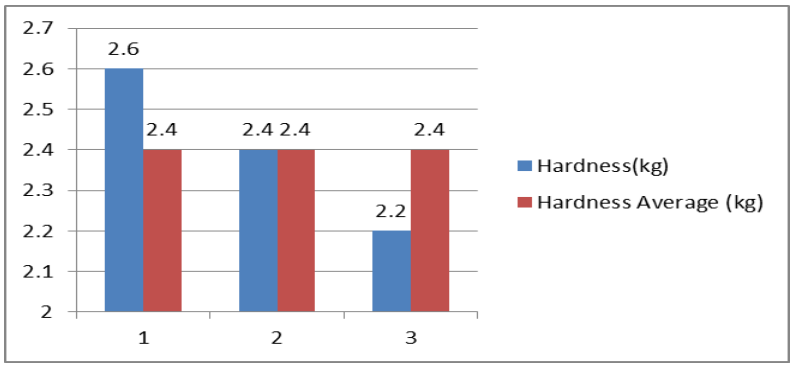

Figure 4.40: Column showing the difference of Hardness (kg) with Hardness Average (kg) of tablets (exposed to normal light for 14 days).

4.1.5.1.4 Data of Friability test

Table 4.41: Friability test of the sample, Exposed to normal light for 14 days

Initial weight	Weight after rotation	Friability
1. 0253	1.0245	0.08%

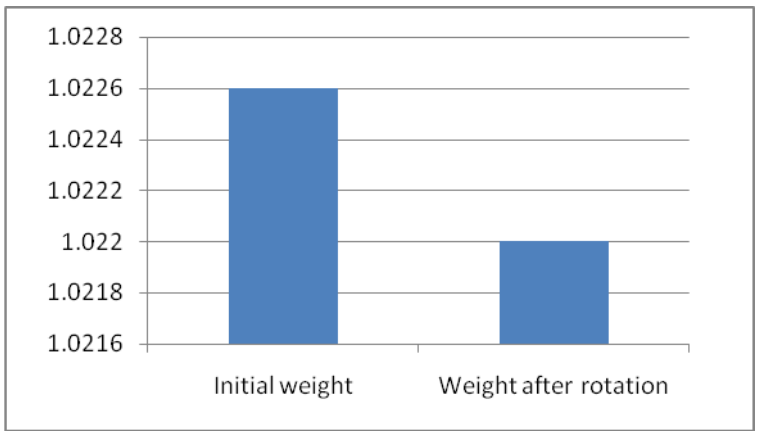

Figure 4.41: Column showing the difference of Initial weight (gm) with Weight after rotation (gm) of tablets (exposed to normal light for 14 days).

4.1.5.2 Samples Exposed to Normal light for 35 Days

10 sample tablets were exposed to normal light source for 35 days. After 35 days samples were collected. Then different physical parameter tests were conducted. Data of these tests are given bellow.

4.1.5.2.1 Data of Weight variation test

Table 4.42: Weight Variation test of the sample, Exposed to normal light for 35 days

Tablet no.	Initial Weight, I(gm)	Average weight A(gm)	% Weight Variation; (A~I/I)×100
1	0.1048		-1.908
2	0.0996		3.2
3	0.1059		-2.927
4	0.1017	0.1028	1.081
5	0.1039		-1.05
6	0.1021		0.685
7	0.1023		0.488

Tablet no.	Initial Weight, I(gm)	Average weight A(gm)	% Weight Variation; (A~I/I)×100
8	0.1007		2.085
9	0.105	0.1028	-2.095
10	0.0973		5.6

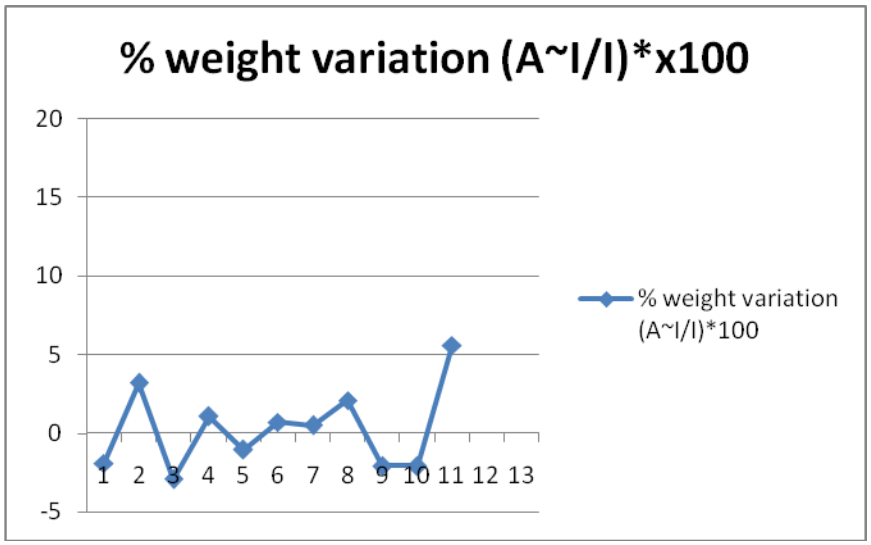

Figure 4.42: Scattered Plot showing weight variation of samples (exposed to normal light for 35 days)

4.1.5.2.2 Data Thickness Test

Table 4.43: Thickness test of the sample, Exposed to normal light for 35 days

Tablet no.	Main scale reading(cm), M	Vernier scale reading(cm), V	Thickness of the tablets (cm), i.e.(M+V) cm
1	0.4	0.09	0.49
2	0.4	0.09	0.49
3	0.4	0.09	0.49

Tablet no.	Main scale reading(cm), M	Vernier scale reading(cm), V	Thickness of the tablets (cm), i.e.(M+V) cm
4	0.4	0.095	0.495
5	0.4	0.09	0.49
6	0.4	0.095	0.495
7	0.4	0.095	0.495
8	0.4	0.095	0.495
9	0.4	0.09	0.49
10	0.4	0.09	0.49

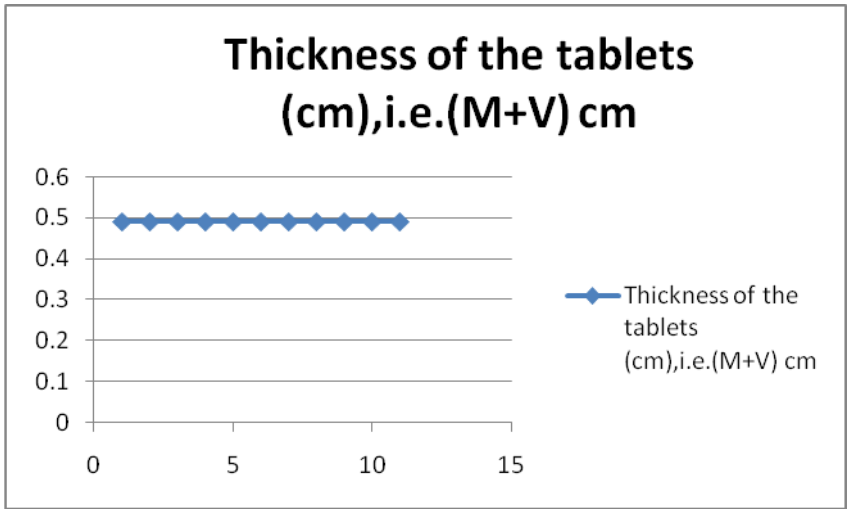

Figure 4.43: Scattered Plot showing thickness of samples (exposed to normal light for 35 days)

4.1.5.2.3 Data of Hardness test

Table 4.44: Hardness test of the sample, Exposed to normal light for 35 days

Tablet no.	Hardness(kg)	Hardness Average (kg)
1	1.8	1.73
2	1.8	1.73
3	1.6	1.73

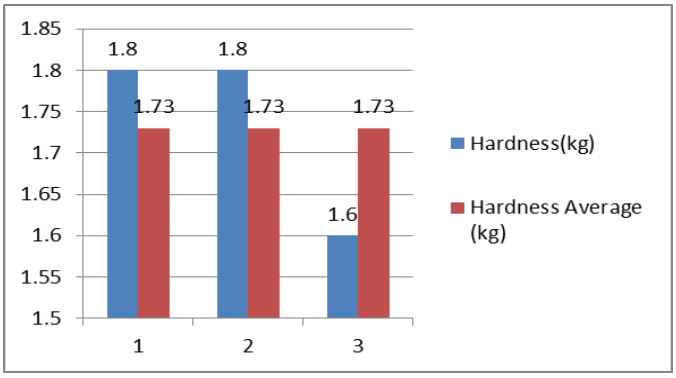

Figure 4.44: Column showing the difference of Hardness (kg) with Hardness Average (kg) of tablets (exposed to normal light for35 days).

4.1.5.2.4 Data of Friability test

Table 4.45: Friability test of the sample, Exposed to normal light for 35 days

Initial weight	Weight after rotation	Friability
1. 028	1.026	0.19%

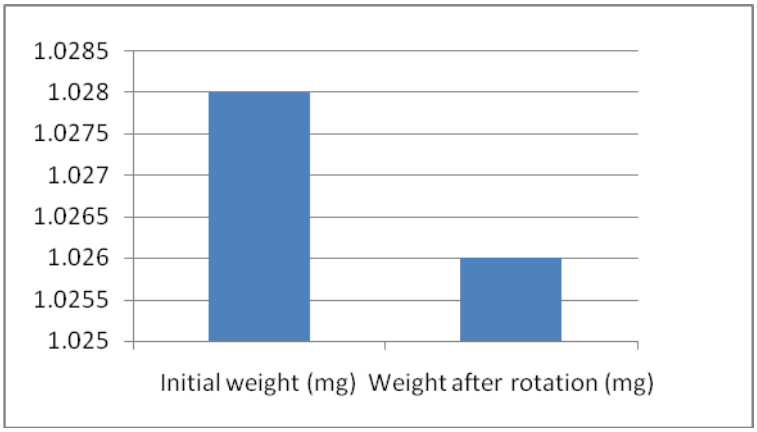

Figure 4.45: Column showing the difference of Initial weight (gm) with Weight after rotation (gm) of tablets (exposed to normal light for 35 days).

4.1.3 Result from Potency Determination by UV- spectroscopy

4.1.3.1 Result from sample that was exposed 25 watt bulb

We found different absorption for different concentration of for Flupentixol dihydrochloride of ANZET in each 3 Hour time interval for sample which was exposed to the 25 watt bulb and we saw that the concentration of Flupentixol dihydrochloride was declined in each three hour time interval.

Table 4.46: Difference in Concentration and Absorbance in each 3 Hour time interval for Flupentixol dihydrochloride

Hours	Absorbance	Concentration (mg/ml)
3	0.743	0.677
6	0.685	0.624
9	0.609	0.554

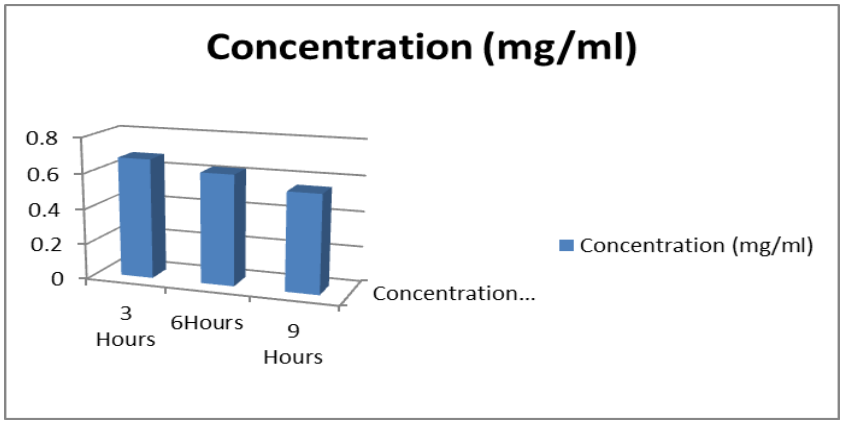

Figure 4.46: Column showing the difference in Concentration after each 3 Hour time interval for Flupentixol dihydrochloride

In case of Melitracen Hydrochloride we found same consequence, We found different absorption for different concentration of for Melitracen hydrochloride of ANZET in each 3 Hour time interval for sample which was kept under the 25 watt electrical bulb andwe saw that the concentration of Flupentixol dihydrochloride was declined in each three hour time interval.

Table 4.47: Difference in Concentration and Absorbance in each 3 Hour time interval for Melitracen hydrochloride

Hours	Absorbance	Concentration(mg/ml)
3	0.550	11.2
6	0.501	10.2
9	0.500	10.17

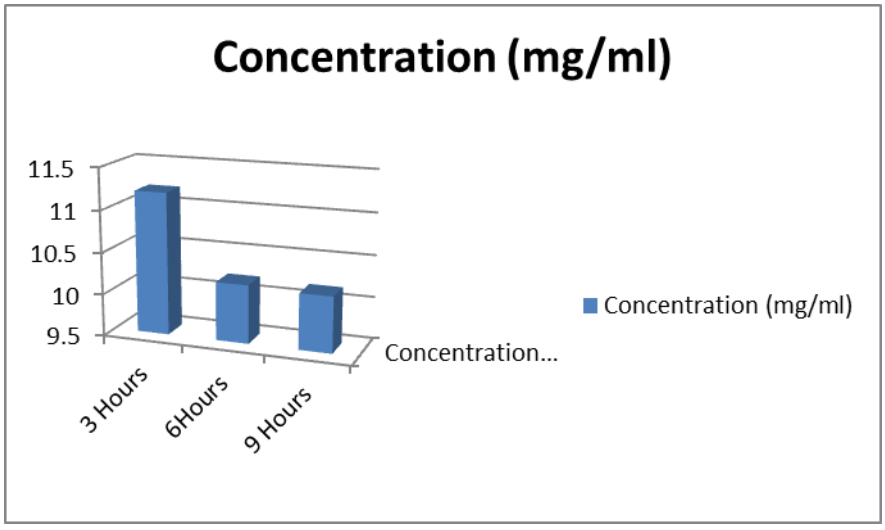

Figure 4.47: Column showing the difference in Concentration after each 3 Hour time interval for Melitracen hydrochloride

4.1.3.2 Result from sample that was exposed 40 watt bulb

We found different absorption for different concentration of for Flupentixol dihydrochloride of ANZET in each 3 Hour time interval for sample which was exposed to the 40 watt bulb and we saw that the concentration of Flupentixol dihydrochloride was declined in each three hour time interval.

Table 4.48: Difference in Concentration and Absorbance in each 3 Hour time interval for Flupentixol dihydrochloride

Hours	Absorbance	Concentration(mg/ml)
3	0.713	0.65
6	0.616	0.56
9	0.575	0.522

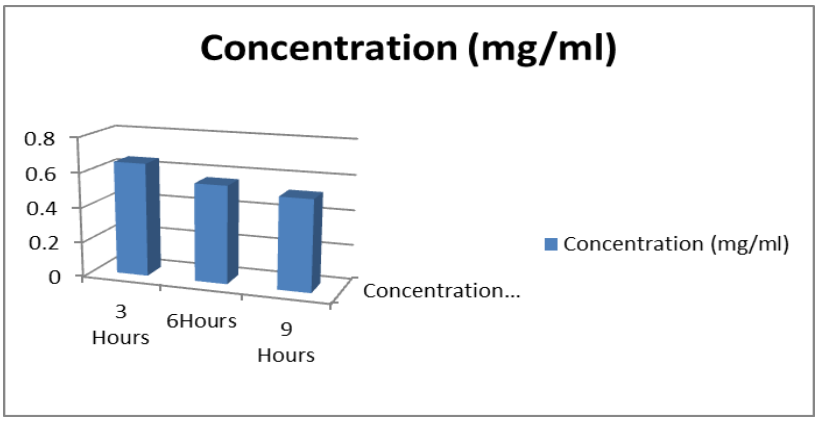

Figure 4.48: Column showing the difference in Concentration after each 3 Hour time interval for Flupentixol dihydrochloride

In case of Melitracen Hydrochloride we found same consequence, We found different absorption for different concentration of for Melitracen hydrochloride of ANZET in each 3 Hour

time interval for sample which was kept under the 40 watt electrical bulb andwe saw that the concentration of Flupentixol dihydrochloride was declined in each three hour time interval.

Table 4.49: Difference in Concentration and Absorbance in each 3 Hour time interval for Melitracen hydrochloride

Hours	Absorbance	Concentration(mg/ml)
3	0.586	11.97
6	0.501	10.2
9	0.478	9.7

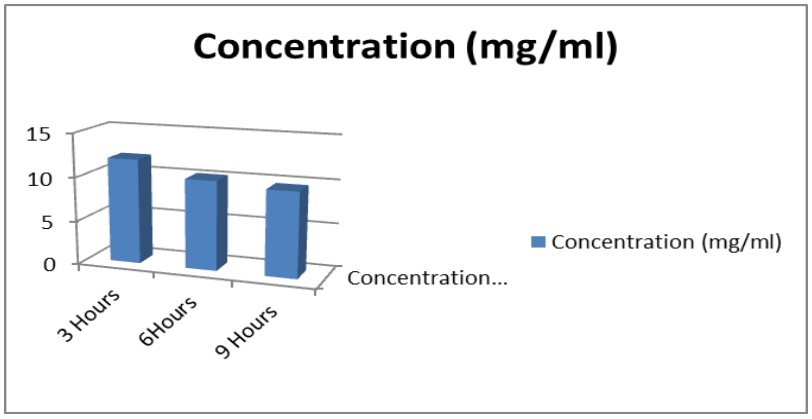

Figure 4.49: Column showing the difference in Concentration after each 3 Hour time interval for Melitracen hydrochloride

4.1.3.3 Result from sample that was exposed Sunlight

We found different absorption for different concentration of for Flupentixol dihydrochloride of ANZET in each 3 Hour time interval for sample which was exposed to the sunlight and we saw that the concentration of Flupentixol dihydrochloride was declined in each three hour time interval.

Table 4.50: Difference in Concentration and Absorbance in each 3 Hour time interval for Flupentixol dihydrochloride

Hours	Absorbance	Concentration(mg/ml)
3	0.676	0.62
6	0.639	0.58
9	0.602	0.55

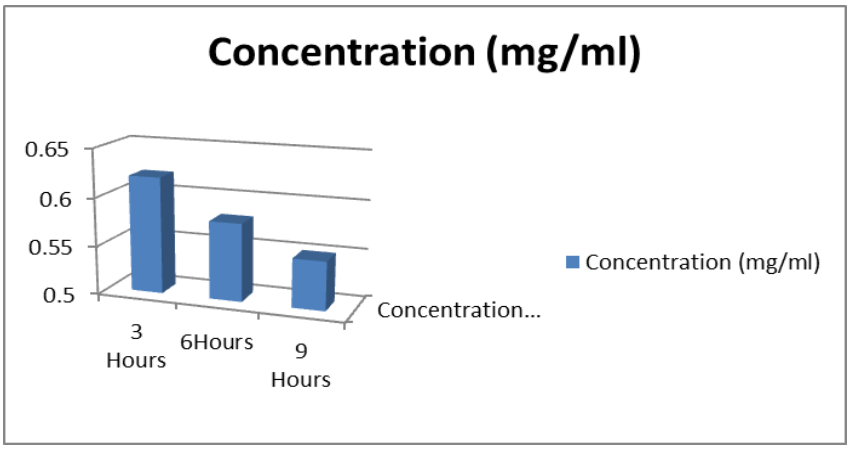

Figure 4.50: Column showing the difference in Concentration after each 3 Hour time interval for Flupentixol dihydrochloride

In case of Melitracen Hydrochloride we found same consequence, We found different absorption for different concentration of for Melitracen hydrochloride of ANZET in each 3 Hour time interval for sample which was kept under the 40 watt electrical bulb andwe saw that the concentration of Flupentixol dihydrochloride was declined in each three hour time interval

Table 4.51: Difference in Concentration and Absorbance in each 3 Hour time interval for Melitracen hydrochloride

Hours	Absorbance	Concentration(mg/ml)
3	0.564	11.5
6	0.536	10.9
9	0.508	10.3

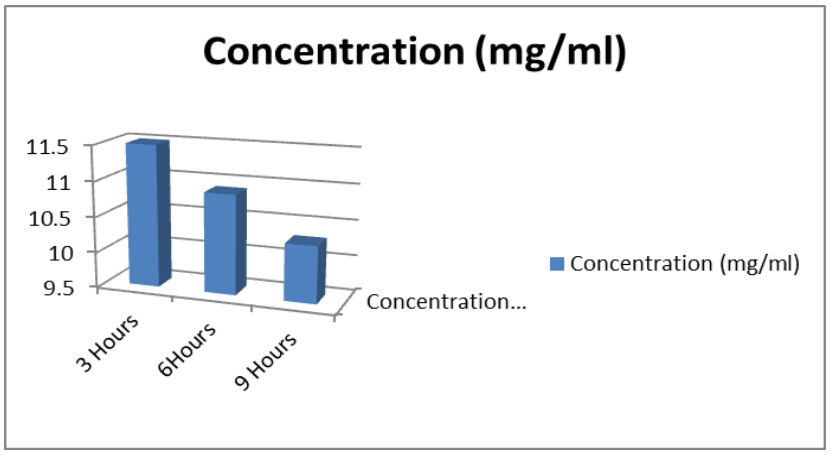

Figure 4.51: Column showing the difference in Concentration after each 3 Hour time interval for Melitracen hydrochloride

4.1.3.4 Result from sample that was exposed normal lightening condition

For our research purpose we have exposed 100 tablets to the normal lightening condition. We put those tablets in a translucent container but we covered it by transparent cling wrap. We took samples after fixed intervals(14, 35 and 49 days) to determine its potency by UV-Spectroscopy. Unfortunately we found some error containing result. From our previous experiments we found that by the affect of light concentration of the drug decreases day by day. But in this experiment when we put the samples in normal light we found after potency determination that, the concentration of drug is increasing. So, this phenomena indicated that

there must be something error or fault in our procedure. Though this part of experiment is a complete failure but here the results of this experiment are given bellow-

Table 4.52: Difference in Concentration and Absorbance in each 3 Hour time interval for Flupentixol dihydrochloride

Week	Absorbance	Concentration(mg/ml)
Week2	0.585	0.53
Week 5	0.886	0.81
Week 7	0.668	0.61

Table 4.53: Difference in Concentration and Absorbance in each 3 Hour time interval for Melitracen hydrochloride

Week	Absorbance	Concentration(mg/ml)
Week 2	0.501	10.2
Week 5	0.512	10.4
Week 7	0.535	10.9

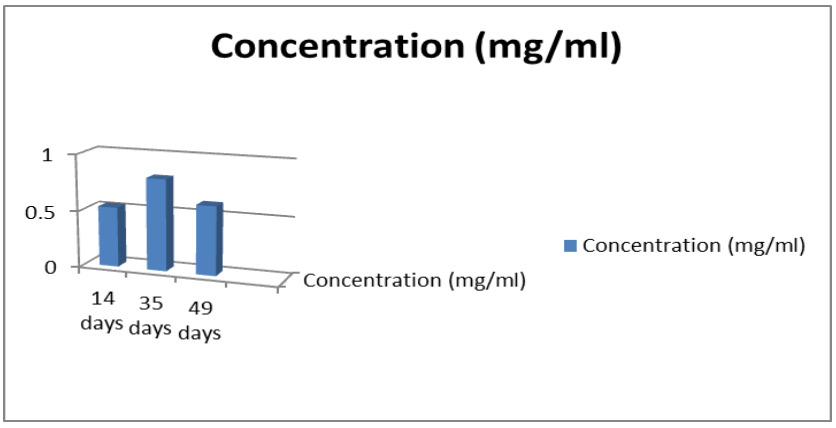

Figure 4.52: Column showing the difference in Concentration after each 3 Hour time interval for Flupentixol dihydrochloride

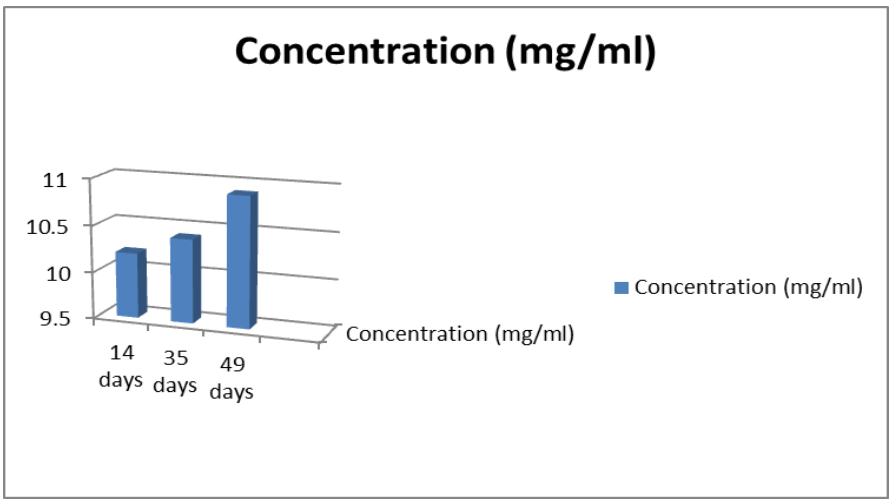

Figure 4.53: Column showing the difference in Concentration after each 3 Hour time interval for Melitracen hydrochloride

4.2 DISCUSSION

4.2.1 Weight Variation Test

In our experiment it was found that the percentage of Weight Variation of the sample tablets was within the accepted range (Weight of tablet 130 mg or less then %error = ±10%) and according to U.S.P. if no more that 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limit the tablet pass the test. So, it is clear that, the light has no effect on weight of the Flupentixol-Melitracen combination drug.

4.2.2 Thickness Test

For all the samples i.e. The Control Sample, Sample that was kept under 25 watts Electrical Bulb, Sample that was kept under of 40 watt Electrical Bulb, Sample that was kept under Sunlight and the Room temperature Sample for stability testing i.e. 14 days Sample, 28 days Sample, 35 days Sample, 45 days Sample the thickness of the tablets remain the same. There was no change in their thickness. So, effect of light does not influence the thickness of Flupentixol-Melitracen combination drug.

4.2.3 Friability Test

Throughout the project, in every experiment we conducted the percentage loss of weight after friability test was so negligible. So, the affect of light has no influence on friability.

4.2.4 Hardness Test

Throughout the research project the hardness of the drug remains in a general range. It was found that the effect of light does not make the tablet fragile. If it does, then the tablet would break by light pressure.

4.2.5 Potency Determination

In our experiment it was found that the concentration of Flupentixol dihydrochloride and Melitracen hydrochloride was decreased gradually in every ovation of light exposure. When sample tablet which was Anzet, kept under the electrical bulb (25 watt and 40 watt) and test every three hour light exposed sample tablet it was found that the concentration of Flupentixol dihydrochloride and Melitracen hydrochloride was decreased gradually. The tablet sample which were exposed six hour on light had less concentration of Flupentixol dihydrochloride and Melitracen hydrochloride than the three hour exposed sample tablet had and also found that nine hour exposed sample tablets have even less concentration of Flupentixol dihydrochloride and Melitracen hydrochloride than three hour and six hour light exposed sample. It was found the same result for the sunlight exposed sample tablets and for the tablets which were kept on normal room temperature condition.

From our research project we can conclude with a decision that, there should be a change in the packaging system of the Flupentixol-Melitracen combination drug product. In present local market most of the available brand of this drug is packaged in plastic transparent blister strip. This package should be opaque thus the light can not pass through the package.

CONCLUSION

In this study it was observed that the physical parameter like weight variation, friability, hardness, thickness have passed the USP and BP specification. But there were remarkable changes in concentration. The concentration of Flupentixol dihydrochloride and Melitracen hydrochloride was decreased gradually after exposure in 25 and 40 watt electrical light condition, sunlight and normal light exposure (room temperature) condition. In this study it was also observed that hardness of six and nine hours 40 watt exposure sample do not meet the USP specification. So we can say that the Anzet containing combination of Flupentixol dihydrochloride and Melitracen hydrochloride is light sensitive and the potency is decreased after light exposure.

REFERENCES

Ahmed, A. Elbary et al. (2011) 'Formulation and Evaluation of taste masked rapidly disintegrating tablet containing Flupentixol Dihydrochloride.' *INTERNATIONAL RESEARCH JOURNAL OF PHARMACY*, Dalia Abd Elaty Mostafa et al. IRJP 2011, 2 (9), 58-64.

Bermudez-Saldana, J.M.et al. 'A micellar liquid chromatographic method for quality control of pharmaceutical preparations containing tricyclic antidepressants.*'Chemistry and Material Science*, Volume 56, Numbers 5-6, 229-306, DOI: 10.1007/BF02491936.

British Pharmacopoeia (2009) Monographs: Medicinal and Pharmaceutical Substances,Flupentixol Hydrochloride, British *Pharmacopoeia,* Volume I, 1 January 2009, The StationeryOffice. London,UK

Che, J. et al. (2007) 'Validation of a sensitive LC/MS/MS method for simultaneous quantitation of flupentixol and melitracen in human plasma.' *Journal of Pharmaceutical and Biomedical Analysis*, Volume 45, Issues 5, Pages 785-792.

Chemblink (2012) Melitracen hydrochloride. *Chemblink* [Online] Available from: http://www.chemblink.com/asp/searching.asp [Accessed 2nd June 2012].

EMC(2012), Flupentixol Tablets, Clinical Particulars[Online] Available from: http:// http://www.medicines.org.uk/emc/medicine/1077 [Accessed 2nd June 2012].

Garay Garcia, L. et al. (2003) 'Simultaneous determination of 4 anti-psychotic drugs in plasma by high performance liquid chromatography application to management of acute intoxication.' *EA2962-Pharmacochimie Université Victor Segalen Bordeaux 2, 146 rue Léo Saignat, Bordeaux Cedex 33076, France*, J Chromatogr B Analyt Technol Biomed Life Sci. 2003 Oct 5; 795 (2): 251-64, 14522030, Cit: 5.

Imran, A. Sheikh et al. (2009) 'Development of Spectrophotometric Method for Simultaneous Estimation of Flupenthixol HCl and Melitracen HCl in Their Combined Dosage Form.' *Asian Journal of Research in Chemistry*, Volume02, Issue 04.

Kirchherr and Kuhn-Velten WN (2006) 'Quantitative determination of forty-eight antidepressants and antipsychotics in human serum by HPLC tandem mass spectrometry: a multi-level, single-sample approach.' *US National Library of Medicine National Institutes of Health*, 2006 Oct 20; 843(1):100-13. Epub 2006 Jun 23.

Kumari, S. et al. (2010) 'Spectrophotometric methods for simultaneous estimation of Flupentixol Dihydrochloride and Melitracen Hydrochloride in combined tablet dosage form.' *Journal of Chemical and Pharmaceutical Research*, J. Chem. Pharm. Res., 2010, 2(3):158-171.

Lakshminarayana, B. (2011) 'Development and validation Methods for the Estimation of Flupenthixol dihydrochloride in bulk and pharmaceutical Dosage Form.' *Rajiv Gandhi University of Health Sciences*, Available At: http://119.82.96.198:8080/jspui/handle/123456789/5016 ((Accessed: 12 May 2012).

McClean, S. et al. (2000) 'Electrospray ionization-mass spectrometric characterisation of selected anti-psychotic drugs and their detection and determination in human hair samples by liquid chromatography-tandem mass spectrometry.' *US National Library of Medicine National Institutes of Health*, 2000 Apr 14; 740(2):141-57.

Mohd, Y. et al. (2011) 'A simple UV spectrophotometric method for the determination of flupentixol dihydrochlodide bulk and pharmaceutical.' *International Journal OF Pharmaceutical Sciences and Research*, Siddiqui et al., IJPSR, 2011; Vol. 2(8): 2152-2155.

Popular-pharma(2012). Anzet, *Advanced Chemical Industries Limited* [Online] Available from: http://www.popular-pharma.com/anzet.htm [Accessed 2nd July 2012].

Roman, M. et al. (2007) 'Quantitation of Seven Low-Dosage Antipsychotic Drugs in Human Postmortem Blood Using LC-MS-MS.' *Oxford Journals,* Volume 32, Issue 2, Pp. 147-155.

Sarah M.R. et al. (2005) 'Development of a solid phase extraction for 13 'new' generation antidepressants and their active metabolites for gas chromatographic–mass spectrometric analysis.' *Journal of Chromatography A,* Volume 1098, Issues 1-2, Pages 19-29.

Shinozuka, T. et al. (2006) 'Solid-phase extraction and analysis of 20 antidepressant drugs in human plasma by LC/MS with SSI method.' *Forensic Science International,* Volume 162, Issues 1-3, Pages 108-112

Sheikh, I.A. et al. (2009) 'Estimation of Flupentixol HCl in single dosage form by RP-HPLC method.' *International Journal of Pharmaceuticals Analysis*, ISSN: 0975-3079, Volume 1, Issue 2, 2009, pp-11-19.

Sharma, M.C. et al. (2010) 'Novel application and spectrophotometric estimation of Melitracen HCl tablet dosage form using Niacin amide as hydrotropic solubilizing agent.' *Journal of Chemical and Pharmaceutical Research*, J. Chem. Pharm. Res., 2010, 2(2): 416-420.

Tanaka, E. et al. (1997) 'Forensic analysis of eleven cyclic antidepressants in human biological samples using a new reversed-phase chromatographic column of 2 μm porous micro spherical silica gel.' *Journal of Chromatography B: Biomedical Sciences and Applications,* Volume 692, Issues 2, Pages 405-412

Usmangani, K. et al. (2011) 'Development of LC Method for the Simultaneous Determination of Antidepressant Drug Combination Melitracen Hydrochloride and Flupentixol Dihydrochloride in their Combined Dosage Form.' *SAGE-Hindawi Access to Research Chromatography Research Internationa*l, Volume 2011, Article ID 632820, 6 pages doi:10.4061/2011/632820.

Wolfgang, W. et al. (2001) 'LC–MS–MS Analysis of the Neuroleptics Clozapine, Flupentixol, Haloperidol, Penfluridol, Thioridazine, and Zuclopenthixol in Hair Obtained from Psychiatric Patients.' *Oxford Journals*, Volume 26, Issue 5, Pp. 303-307.

Walter, S. et al. (1999) 'Quantification of the antipsychotics flupentixol and haloperidol in human serum by high-performance liquid chromatography with ultraviolet detection.' *Journal of Chromatography B: Biomedical Sciences and Applications*, Volume 720, Issues 1- 2, Pages 231-237.

Wille, S. (2008) 'Quantitative analysis of new generation antidepressants using gas chromatography-mass spectrometry.' *The degree of Doctor in Pharmaceutical Sciences, Ghent University Faculty of Pharmaceutical Sciences*, Available At: http://jat.oxfordjournals.org/content/26/5/303.abstract (Accessed 29 may 2012).

Xu, P. et al. (2008) 'Validated Liquid–Liquid Extraction and LC–ESI–MS Method for the Determination of Melitracen in Human Plasma.' Online publication 18 April 2008, Available At: http://www.springerlink.com/content/8x68345412h780x5, (Accessed: 29May 2012)

Ying, H. et al. (2010) 'Quality Index Evaluation Method for Quality Analysis of Flupentixol and Melitracen Tablets.' *Chinese Journal*, Category Index: R927.2, DOI: CNKI: SUN: ZGYA.0.2010-01-033.

Zuo, X. et al. (2009) 'LC–ESI–MS Determination of Flupentixol in Human Plasma.' *Chromatographia (February 2009)*, 69 (3-4), pages 301-305